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CHRONIC RELAPSING FEBRILE NODULAR NONSUPPURATIVE PANNICULITIS (WEBER–CHRISTIAN DISEASE)*

Relation to Rheumatic Fever and Allied Diseases

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CHRONIC relapsing febrile nodular nonsuppurative panniculitis is a disease of unknown etiology characterized by recurrent fever associated with a nodular nonsuppurative inflammatory process with necrosis of the subcutaneous and sometimes internal fatty tissue. The nodules occur singly or in clusters varying in diameter from 1 to 12 cm. The process can occur in all parts of the body but particularly on the thighs. The fever persists as long as there are nodules present. These nodules may be painless, particularly if small, or tender, especially when large. The overlying skin is red and raised but is not attached to the subcutaneous tissue. When involution occurs, the overlying skin becomes pigmented, and the nodule shrinks in size, leaving a depressed area.

The microscopical picture varies according to the stage in which the biopsy is taken. In the early stages there is edema, exudation, congestion and infiltration with segmented cells but no suppuration. The fat cells show collapse of the cell membrane. There is a necrosis of fat. An invasion of large histiocytes phagocytic for fat follows. These cells are characterized by a large, irregular nucleus and a frothy cytoplasm because of the ingestion of fine fat droplets. By confluence of several macrophages giant cells, containing 10 to 12 nuclei, are formed. In addition, there is an infiltration by lymphocytes. In the later stages there is replacement by collagen, and fibrosis finally dominates the picture.

CASE REPORT

A 29-year-old secretary was admitted to the hospital on February 2, 1949, because of migratory joint pains and fever. Two weeks prior to admission, the patient had a sore throat, followed in 1 week by migratory joint pains and fever, for which her physician sent her to the hospital with a tentative diagnosis of acute rheumatic fever. She had been well until February, 1935, when she had migrating joint pains and fever accompanied by purpura, which the consulting hematologist considered to be associated with rheumatic fever. In December, she was readmitted to the hospital with a diagnosis of Henoch's purpura. In January, 1936, an appendectomy was performed. On the fourth admission, in 1938, for joint pain and fever, a 7-foot film of the chest revealed a slight bulge of the left auricle. In 1943 leukopenia developed when sulfadiazine was given prophylactically for rheumatic fever. In 1944, sulfapyridine was given in small doses, but again leukopenia developed. In 1948 the patient was admitted on two occasions for cystitis.

The patient's mother had rheumatoid arthritis, and her maternal aunt had diabetes. Otherwise, the family history was noncontributory.

Physical examination revealed a well nourished, well developed woman who complained of pain in the elbows, left shoulder and right knee of 1 week's duration. The skin was clear and moist. The neck showed stiffness and limitation of motion. The heart was normal to percussion, the rhythm was regular, and there was a Grade II systolic murmur at the mitral area, with a presystolic rumble. The lungs were clear. The abdomen was soft and nontender, and no masses could be felt. The extremities demonstrated swelling and tenderness of the right knee.

The temperature was 100°F., and the pulse 100. The blood pressure was 106/70.

Examination of the blood disclosed a red-cell count of 4,050,000, with a hemoglobin of 11.7 gm., and a white-cell count of 14,550, with 7 per cent band cells, 83 per cent segmented cells, 3 per cent eosinophils and 7 per cent lymphocytes. The erythrocyte sedimentation rate (Wintrobe method) was 48 mm. in 1 hour. Urinalyses showed a trace of albumin with 1 to 3 white blood cells per high-power field in the sediment. An electrocardiogram revealed a normal sinus rhythm at a rate of 90, PR intervals of 0.18 to 0.20 second, normal T waves in all leads and left-axis deviation. On the next day, the PR interval was 0.20 to 0.21 second, and the T waves in Leads 2 and 3 were diphasic. These observations were suggestive of myocardial changes. X-ray examination of the heart demonstrated a barium-filled esophagus displaced posteriorly, suggesting a slight enlargement of the left auricle; the horizontal cardiac measurement was 12.8 cm., and the internal diameter of the chest was 27.5 cm. The spine showed scoliosis convexity to the right.

During the first week of hospitalization the temperature ranged from 99.4 to 100.4°F., and the pulse rate from 90 to 100. The left elbow and shoulder became free of pain. The right knee had become swollen and tender within 24 hours, but these symptoms subsided after 5 days. After a period of 3 weeks all joint symptoms and signs had disappeared. The temperature ranged from 98 to 99.4°F., and the pulse rate from 80 to 90. The murmur in the mitral area disappeared. The white-cell count numbered 7100 to 8000. The sedimentation rate became normal.

On March 3 a painful raised nodule 3 cm. in diameter on the medical aspect of the right thigh, 4 cm. above the knee, developed. This lesion involved the subcutaneous tissue. The overlying skin was red. On March 8 a second lesion, 4 to 6 cm. in diameter, appeared just above the first, followed

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by a third lesion, 2 cm. in diameter, just above that. Accompanying these lesions was a rise in temperature from 99.8 to 101°F., headache, malaise, anorexia and muscle pain. A surgical consultant suggested the diagnosis of thrombophlebitis of the external saphenous vein. Within 48 hours, a crop of new lesions, consisting of subcutaneous nodules with redness of the overlying skin, appeared on the lateral and posterior aspects of the right thigh. In addition, new lesions appeared on the left thigh, varying in size from 3 to 12 cm. in diameter. The overlying skin was not attached to the lesions except in the large nodules during the early stage of development. The lesions underwent involution, and within 12 to 14 days there was pigmentation of the skin. There were 35 nodules in various stages of development during an observation period of 3 months. By June 15 all lesions had undergone involution, and no new lesions had appeared (Fig. 1). The patient felt better. Definite depressions were noted at the site of the large lesions and on palpation of these depressions nodules could be felt underneath.

FIGURE 1. *Multiple Lesions of Panniculitis in Various Stages of Evolution and Involution.*

Note the nodules on the lateral aspect of the left thigh and also the pigmented central depression as a result of healing, the early large nodule on the medial aspect above the right knee and the numerous depressions on the anterior and medial aspects of the right thigh.

During the period of panniculitis the white-cell count ranged from 6500 to 12,500, with 60 to 70 per cent segmented cells, 0 to 4 per cent eosinophils, 10 to 23 per cent lymphocytes and 7 to 12 per cent monocytes. The sedimentation rate was normal. Electrocardiographic tracings were normal, the heart rate ranging from 80 to 90. Repeated urinalyses were normal. On concentration of the urine the specific gravity was as high as 1.033, and on dilution it was as low as 1.001. Agglutination tests for brucellosis were negative. The differential agglutination titer for rheumatoid arthritis was 80 units. The antistreptolysin titer just before discharge was 125 units. The total cholesterol was 192 mg., the cholesterol esters 143 mg., the total fat 616 mg., and the neutral fat 32 mg. per 100 cc.

The first biopsy, taken on April 16 from a lesion on the lateral aspect of the right thigh, showed a piece of skin with subcutaneous tissue. The underlying fatty tissue was 2 cm. thick. The color was gray, and the consistence was firm.

On microscopical examination the epidermis had a fairly large amount of horn substance covering the surface. Demarcation was good. The papillae were partly slender and partly broad. The basal layer was pigmented. Skin appendages were preserved. In the subcutaneous fatty tissue there were rather large areas of poorly demarcated cellular exudate. The infiltrate was of varying density and consisted of a large variety of cellular elements. Monocytes, lymphocytes, a moderate number of plasmocytes, segmented cells and some giant cells of the foreign-body type were seen. There were many large, oval-shaped cells, which had a foamy acidophilic cytoplasm and a dense, dark-stained, round nucleus located either in the center of the cell or near its edge. The intracellular material was finely granular and stained black with osmic acid, indicating the material to be lipid (see Fig. 5). At the borders of the granuloma nodules young fibroblastic elements were seen arranged in winding bundles, apparently penetrating toward the center and replacing the necrotic fatty tissue.

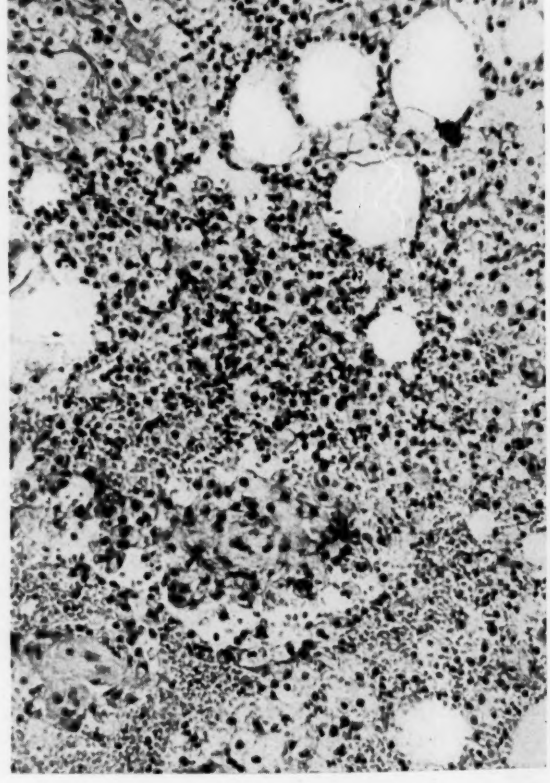

FIGURE 2. *Early Stage of Panniculitis (from the Second Biopsy Taken within Thirty-Six Hours of the Appearance of the Nodule).*

Note the pleomorphic character of the exudate.

The diagnosis was extensive necrosis of subcutaneous fat with nonspecific granulation and connective tissue, compatible with nodular panniculitis (Weber–Christian disease).

On the basis of bacterial allergy, penicillin, 1,800,000 units daily for 21 days, followed by streptomycin, 2 gm. for 10 days, and aureomycin, 2 gm. daily for 5 days, were given with no effect on the lesions. Three minims of epinephrine, 1:1000 dilution, given intramuscularly every 4 hours, shortened the period of involution from 14 days to an average of 4 days but did not prevent the development of new lesions. This drug was discontinued, however, because of unpleasant side effects. From June 15 until discharge in July the patient felt better.

A week after discharge from the hospital a new lesion appeared on the anterior right thigh, 10 cm. above the knee, accompanied by fever and malaise. The nodule measured 2 cm. in diameter and as it underwent involution the temperature subsided. Examination of both thighs showed pitting and depressions of the skin in 30 areas, chiefly on the lateral and medial aspects. Underlying the depressed areas, nodules could be felt. Some of the recent nodules had caused the skin to be raised. The biopsy incision, which was 3½ months old, was still not entirely healed. Examination of the heart showed no abnormalities.

On August 8, after a few days of increased activity, a large lesion developed on the inner aspect of the right thigh, enlarging rapidly to 8 cm. in diameter. On the next day a second lesion appeared on the lateral aspect of the left thigh, 5 cm. in diameter, accompanied by a rise in temperature, malaise and joint pains. New nodules appeared on both thighs, some nontender and others large and tender. From August 12 to September 15 new nodules appeared, accompanied by a temperature ranging from 99 to 103°F. A nodule on the left thigh was accidentally struck, and this was followed by a copious drainage of fatty globules. The patient noted that increased activity was followed by the appearance of new lesions. She frequently complained of aches in the shoulders and right hip during the appearance of these lesions.

From the time of discharge to the present there has been a gradual darkening of her hair, although her family are all blondes.

On August 12 a second biopsy was taken of a nodule in the early stage of development on the medial aspect of the right thigh. The specimen consisted of a rectangular piece of skin with underlying fat, 3 by 2 cm. in diameter.

Microscopical examination showed adipose tissue with extensive inflammatory reaction and with multiple foci of necrosis. The infiltration was partly nodular and partly diffuse. Creeping between the fat cells and separating them from each other was infiltration by lymphocytes, which were seen even within the membrane of the fat cells. Accompanying the cellular infiltrate was massive exudation of apparently liquid material, which accepted a pink color in sections stained with hematoxylin and eosin. In comparison with sections from the previous biopsy, lipophages and giant cells were more numerous. The infiltrate was frequently perivascular, and the vessel wall seemed thickened. No fibrosis was present (Fig. 2-4).

The diagnosis was acute panniculitis.

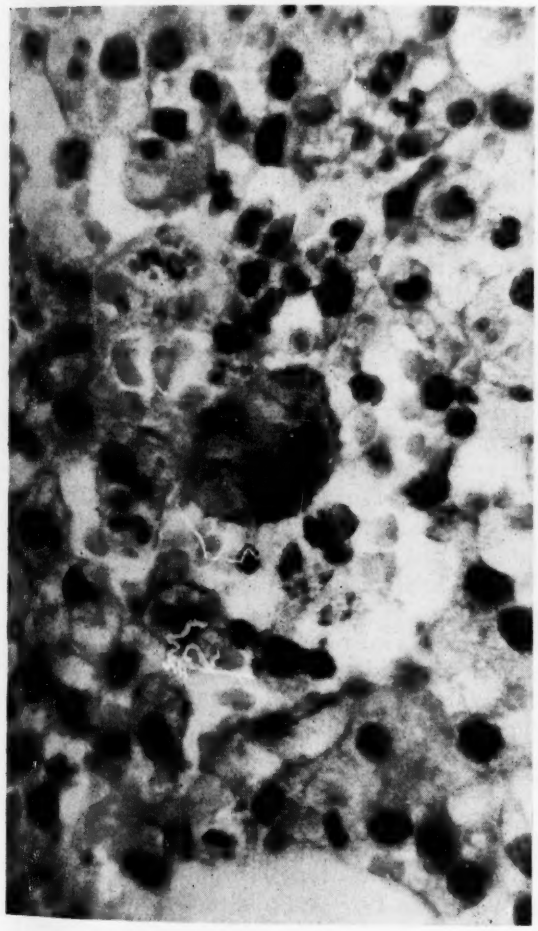

FIGURE 3. *High-Power View of a Portion of the Specimen Shown in Figure 2 (at Top).*

Note the numerous lipophages, with foamy cytoplasm, giant cell and few granulocytes.

FIGURE 4. *High-Power View of the Early Lesion (from the Second Biopsy).*

Note the perivascular exudate, infiltration of intercellular spaces and invasion of the damaged fat-cell membrane by lymphocytes.

Discussion

Weber–Christian disease, although not common, has been described and reviewed in recent years.[1-7] Thirty-six cases have been reported up to the present time. The clinical and pathological features have been described, and suggestions for treatment have accompanied these reports. The first case of nodular panniculitis was reported by Pfeiffer[8] in 1892, and the second case by Gilchrist and Ketron[9] in 1916.

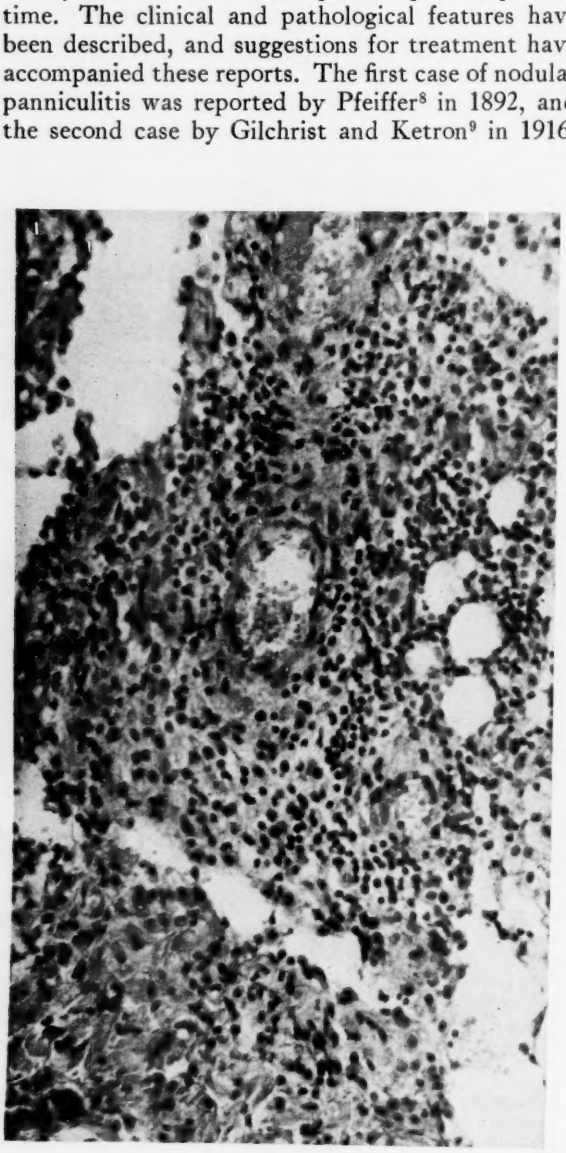

Figure 5. *Healing Stage of Panniculitis (from the First Biopsy).*
Note the increase in connective tissue, marked foreign-body reaction and lesser number of lipophages in comparison with the early lesion.

Weber,[10] in 1925, and Christian,[11] in 1928, reporting the third and fourth cases, respectively, introduced the term chronic relapsing febrile nodular nonsuppurative panniculitis, because it was descriptive of the outward manifestations of the disease.

Many factors have been implicated by previous authors to explain the etiology, but definite proof is still lacking. The reports fall into two general groups; bacterial infection and drug sensitivity. Pfeiffer,[8] described focal infection preceding panniculitis. A Russian pathologist, Abrikossoff,[12, 13] in 1926, observed nodules in obese persons during convalescence from infectious diseases, especially relapsing and typhus fevers. The lesions were not only in the panniculus adiposus but also in the retroperitoneal omental and mesenteric fat. The process described as multiple granulomas was similar to that seen in Weber–Christian disease.

Alderson and Way,[14] in 1933, presented the fifth case of nodular panniculitis after an abscess. Netherton,[15] in the same year, reported this disease in a woman after tonsillectomy, cholecystectomy and appendectomy. In 1938 Puente[16] described panniculitis in a patient with a staphylococcal infection.

Bailey,[17] in 1937, and Larkin,[2] in 1944, noted that removal of infected foci did not prevent fat necrosis. Skiöld[18] found that removal of foci was followed by a greater dissemination of the lesions.

Spain and Foley[3] noted at post-mortem examination that the nodules involved not only the subcutaneous fat but also the mesenteric omental and pretracheal fat. Ungar[19] reported a case of Weber–Christian disease in a thirty-seven-year-old man who died of suppurative peritonitis. At autopsy, the characteristic lesions were found throughout the adipose tissue; the author suggested a blood-borne noxa as a cause.

Arnold,[20] on the basis of bacterial allergy, gave sulfapyridine and reported remission. Pierini and his associates[5] suggested that the disease represents a nonspecific process associated with infection of the nose and throat. Rist and Renault[21] considered Weber–Christian disease as a response to different allergens.

Weber[22] found relapse in 1 patient after long ingestion of iodides, and 2 of Bailey's[17] cases were also related to iodides. The patient of Mostofi and Engleman,[23] a Filipino soldier, gave a history of ingestion of quinacrine and quinine, antimony, sulfadiazine and penicillin.

Although bacterial infection or drug sensitivity has received prominence as an explanation by recent authors, a relation to rheumatism was suggested by Weber[10] in 1925 and by Stockman[24] in 1928. The latter considered panniculitis as a fibrositis of adipose tissue. On the other hand, joint pain can accompany Weber–Christian disease and confuse the picture with rheumatic fever[19] or disseminated lupus.[25]

Duran–Reynals[26] compared Weber–Christian disease with necrotizing disease of the fatty and muscular tissue. He found in rabbits that the clinical phase could be brought about by a variety of nonspecific substances or stimuli such as viruses, bacterial products, saline solutions and tissue extracts. In rabbits not sensitized the disease could not be brought about.

Summary

The thirty-seventh reported case of chronic relapsing febrile nodular nonsuppurative panniculitis is presented, with a clinical and histologic picture typical of the disease. An unusual feature was the appearance of the disease in a patient with a history of rheumatic fever. There was also a history of sensitivity to drugs.

Although the occurrence of rheumatic fever and Weber–Christian disease in the same patient may have been coincidental, there is the possibility that in this case the two diseases represented a common background. The theory is advanced that in Weber–Christian disease the antigen-antibody reaction may result in destruction of the cell membrane and liberation of free fat. The antigen, which originally may be a chemical, a protein or a bacterial product, stimulates formation of an auto-antibody. The auto-antibody, reacting with the antigen or antigen-complex in the fatty tissues, leads to nodular panniculitis.

Weber–Christian disease is regarded not as a disease entity but rather as an allergic systemic reaction to nonspecific stimuli, with focal manifestations in the subcutaneous or intraperitoneal fat, resulting in destruction of the supporting framework of the fat cell and liberation of free fat.

It is suggested that nodular panniculitis (Weber–Christian disease) is allied to the group of collagen diseases.

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POSTOPERATIVE POTASSIUM DEFICIT AND METABOLIC ALKALOSIS (Concluded)*

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DISCUSSION

Evidence of a Tissue Potassium Deficit

Hypochloremia resistant to correction by isotonic sodium chloride solution has previously been observed in postoperative patients. Ten years ago, Maddock[3] described a group of patients who demonstrated a resistant hypochloremia after operation. Chloride administered as the sodium salt was either excreted in the urine or added to the body with water. These patients exhibited lethargy, depression, weakness, fatigue, anorexia, nausea, dehydration, drowsiness and stupor. Clinical improvement and rise in plasma chloride occurred when the patients started to eat. No explanation was offered. Ariel and his co-workers[4] again called attention to this group of patients, emphasizing in addition the occurrence of abdominal distention. Elevated serum carbon dioxide combining power and lowered serum proteins were noted in all their cases. In 3 of their 5 cases a rise in serum chloride and fall in serum carbon dioxide combining power were related to the resumption of a diet. In retrospect, it appears that these patients with hypochloremic alkalosis had a potassium deficit that was corrected by the provision of dietary potassium. Howard and Carey[10] have demonstrated that large amounts of sodium chloride or ammonium chloride are ineffective in raising serum chloride and lowering serum carbon dioxide when potassium deficit is present.

The co-existence of intracellular potassium deficit and metabolic alkalosis has been demonstrated both experimentally and clinically by Darrow and his co-workers,[25-27] who have observed that in rats made potassium deficient by several means, an excellent correlation exists between the degree of alkalosis (serum bicarbonate elevation) and the lowering of muscle potassium content. An increase of muscle sodium coincident with the potassium loss was also observed. It has been shown that the alkalosis and potassium deficit in such rats can be accounted for by a diuresis of potassium and frequently of chloride, and a retention of sodium relative to chloride.[28] Simultaneous expansion of the radiosodium space and reduction of the chloride content have also been demonstrated in these animals.[28] The space determinations in Case 1 (Fig. 3) confirm the existence of the same relations in the human being. In this patient there was an increase in extracellular fluid sodium content with respect to chloride on the second postoperative day, compared to the preoperative values. This coincided with a rise in serum pH and carbon dioxide content. On the fifteenth postoperative day, when symptoms and serum electrolyte changes were maximal, there was a definite shrinkage of the extracellular fluid volume as measured by bromide space and of the chloride contained therein. There was at the same time a striking enlargement of the sodium space and a comparable increase in its sodium content. The amount of sodium that could then be accommodated in the bromide (chloride) space was in excess of the amount usually associated with chloride, thus fixing the necessary conditions for metabolic alkalosis. There was an increase of serum bicarbonate (carbon dioxide, 41 millimols per liter) to cover the excess base. The sodium that could not be accounted for in the chloride space amounted to over 700 milliequiv. It is assumed that most of this excess sodium migrated into the cells to replace lost potassium. If this represents the magnitude of intracellular potassium loss, it is easy to understand why repletion was slow, since potassium was administered at the rate of 40 to 60 milliequiv. per day. The significant fall in erythrocyte potassium and rise in erythrocyte sodium that this patient showed (Table 2, Case 1) support this interpretation of the space data.

The sodium retention demonstrated by the space determinations and by balance studies[29] probably accounts for the water retention (edema) and at least some of the hypoproteinemia observed in our cases. Provision of potassium results in a diuresis of sodium and water, disappearance of edema and rise in serum protein. Disruption of the operative wound and evisceration occurred in 2 patients (Cases 11 and 12) after potassium deficit had developed. This suggests that potassium deficit or resulting edema of the suture line, or both, may interfere with wound healing.

The development of metabolic alkalosis and of intracellular potassium loss and sodium gain was considered by Darrow et al.[27] to be the result of a biologic equilibrium that is attained in the presence of normal renal function when there is loss of a single ion such as potassium or chloride. Interference with renal function by severe infection or urinary-tract obstruction or loss of multiple ions in intestinal fluids might be expected to prevent attainment of this equilibrium, as was apparently ob-

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served in the cases of hypopotassemia, described above, in which alkalosis or hypochloremia failed to develop.

Hypochloremic alkalosis is frequently found after excessive loss of gastric juice.[30] Moyer[31] has recognized the existence of intracellular potassium loss under these circumstances. Low serum potassium levels have been reported in a number of cases of gastric alkalosis.[8, 9, 32-35] A marked lowering of red-cell potassium was reported by Kennedy et al.[34] in a patient with alkalosis and hypopotassemia due to loss of intestinal fluids. We have also observed significant lowering of erythrocyte potassium concentration in 2 of 5 patients, referred to above, with postoperative potassium deficit and metabolic alkalosis (Table 2). Low serum potassium levels are usually associated with a deficit of intracellular potassium.[8] Mudge and Vislocky[9] have shown a low muscle potassium content in 2 patients with alkalosis, hypochloremia and hypopotassemia resulting from excessive loss of gastrointestinal fluids. All the patients in our series had serum potassium levels below 3.8 milliequiv. per liter, the lowest being 1.9 milliequiv. It is reasonable to assume, therefore, that all the patients reported here probably had intracellular potassium deficits.

Loss of potassium in excess of the amount expected from loss of nitrogen is presumptive evidence of intracellular potassium deficit, and has been observed during the immediate postoperative period by several authors.[36-40] There seems to be a general correlation between the severity of the operation and the magnitude of the potassium loss. Retention of administered potassium, in excess of that expected from nitrogen stored, has likewise been accepted as presumptive evidence of antecedent deficit and has been demonstrated in patients who exhibited hypochloremia, metabolic alkalosis and hypopotassemia postoperatively.[8, 10]

We have observed potassium losses in excess of nitrogen in 2 patients after operation. These data will be presented in detail elsewhere.[29] The deficit arises largely during the first few postoperative days, as a result of renal loss of potassium. There may be an accompanying loss of chloride in the urine, which, in relation to sodium excreted, is in excess of the ratio of 1:1.26 at which these two ions exist in extracellular water, or there may be chloride retention, with a relatively greater retention of sodium.[7, 41] These changes result in the development of metabolic alkalosis, with elevation of serum pH and carbon dioxide content.

The dramatic reversal of symptoms, electrocardiographic changes and chemical abnormalities by administration of potassium is well illustrated in Cases 1, 2 and 3. Potassium retention during recovery has been demonstrated by our balance studies and others already cited. Lowe et al.[41] have shown, in children following operations for perforated appendixes or for intussusception, that potassium administered during the postoperative course prevents the loss of intracellular potassium and of chloride in excess of sodium. By providing 50 milliequiv. per day of potassium to 4 adults, Randall and his co-workers[11] were able to prevent potassium loss after relatively atraumatic procedures. It therefore appears that a deficit of potassium is of primary importance in the pathogenesis of the syndrome.

Relation of Electrocardiographic Changes to Potassium Deficit

Lowered amplitude of T waves, depression of ST segments and prolongation of the QT interval, in association with low serum potassium levels, have been found in recovery from diabetic acidosis,[42] familial periodic paralysis,[43] chronic nephritis,[44] after excessive loss of intestinal contents and postoperatively.[8, 33] The occurrence of ectopic rhythms (ventricular premature beats and nodal rhythm) with potassium deficit has not previously been emphasized. Bigeminal rhythm has been produced in a patient with familial periodic paralysis by the administration of a large quantity of glucose, with a subsequent fall in serum potassium concentration.[45]

The observed electrocardiographic changes are probably due to myocardial potassium deficit. Orent-Keiles and McCollum[46] demonstrated that rats on very low potassium diets died apparently from cardiac lesions. The animals showed reduced potassium content of the heart muscle and necrosis and scarring of muscle fibers. Pearson and his coworkers[47] obtained electrocardiograms from potassium-deficient rats that exhibited lowered amplitude of the T waves and interference with auriculoventricular conduction.

Lowered amplitude of the T waves coincident with the development of alkalosis and hypochloremia, but preceding a fall in serum potassium, was observed in Cases 1 and 21. The latter patient was known to be potassium deficient on the basis of balance studies. We are inclined to believe, therefore, that the electrocardiogram may in certain cases be a better index of tissue potassium deficit than the serum potassium level. This would fit observations that there may be considerable tissue losses of potassium without depletion of extracellular potassium.[8, 29] The delayed return of the T waves in Case 1 after administration of potassium suggests that the tissue potassium deficit must have been large. The delayed return of serum potassium to normal and the large increase in intracellular sodium demonstrated by space studies fit with this supposition.

The almost invariably lowered amplitude of T waves that occurred in the cases reported here suggests that this change may be used in the diagnosis of potassium deficit, particularly if serum potassium levels are not readily obtainable. Confirmatory

evidence can usually be found in the presence of elevated serum pH and serum carbon dioxide content, and hypochloremia. The presence of myocardial lesions or the administration of digitalis will obscure electrocardiographic changes from potassium deficit.

Pathogenesis of Postoperative Potassium Deficit

Potassium deprivation. All the patients in this study, except 1, were on a low intake of potassium postoperatively. Adults on a normal intake who are abruptly deprived of potassium will continue to excrete potassium in the urine in excess of that expected from the nitrogen balance. This loss may amount to about 20 to 50 milliequiv. on the first day and gradually decreases thereafter.[8, 11] Such losses undoubtedly were an important factor in the development of the deficits described. However, it appears that potassium deprivation alone does not account for the magnitude of some of the postoperative potassium losses observed,[39, 48, 49] the great rapidity with which potassium deficit sometimes develops (Case 2 and 29) or the development of deficit in patients who are being maintained on a constant or adequate potassium intake (Case 30).[48-52]

Water and sodium chloride intake. Large infusions of glucose or a large intake of sodium chloride, either parenterally or orally, will induce losses of intracellular potassium.[39, 49, 53, 54] Sodium chloride appears to cause substantially larger losses than glucose in water.[29, 53] MacInnes, Bodansky and Brunschwig[55] observed low serum potassium levels preoperatively in 2 patients that were ascribed to the possibility of excessive parenteral fluid administration. One of our patients (Case 2), however, received no saline solution whatever and only modest amounts of glucose in water. The majority of the patients described here did not receive excessive parenteral administration of glucose or saline solution.

Loss of gastrointestinal secretions. Metabolic alkalosis produced by excessive withdrawal and inadequate replacement of chloride from the stomach results in a potassium deficit, as mentioned above, but this factor was not significant in the majority of the cases. Loss of potassium in gastrointestinal fluids was likewise not significant in most cases. Dehydration[56] has been shown to induce potassium loss, but was not a prominent feature.

Malnutrition. Howard and Carey[10] have emphasized the possible role of prior malnutrition and potassium depletion in the development of postoperative potassium deficit. Malnutrition or marked weight loss was evident in only a few of the patients.

Adrenocortical hyperfunction. The muscular weakness and electrolyte changes observed in the postoperative syndrome resemble distinctly the findings in some patients with Cushing's syndrome (hyperadrenocorticism) in which low serum and muscle potassium, together with metabolic alkalosis and hypochloremia, has also been found.[57, 58, 58a] Improvement in muscular strength, reversal of the electrolyte changes and retention of potassium have been noted upon administration of potassium chloride to patients with Cushing's syndrome.

Lowered muscle potassium, increased muscle sodium and metabolic alkalosis have been produced in rats by the administration of desoxycorticosterone acetate either alone or with a potassium-deficient diet.[27] Hypopotassemia, hypochloremia and elevation of serum carbon dioxide have been found in a patient with Addison's disease receiving desoxycorticosterone.[59]

Hypopotassemia and metabolic alkalosis have also been produced in patients by the injection of adrenocorticotrophic hormone (ACTH)[60-62] or Cortisone.[63] Of 33 patients who received ACTH or Cortisone for the treatment of neoplastic diseases at this hospital, hypopotassemia developed in 15 and metabolic alkalosis in 10 within three to twenty-three days of the start of therapy.[64] Those with hypopotassemia exhibited symptoms and electrocardiographic changes identical to those in the postoperative group. There was profound muscular weakness in 1 patient. Studies on several of these patients revealed losses of potassium and phosphorus is excess of nitrogen, retention of sodium relative to chloride, hypochloremia, a fall in the eosinophil count to 0, or near 0, and increased excretion of ketosteroids and reducing steroids.

Metabolic and clinical changes similar to those produced by ACTH and Cortisone have also been observed in balance studies on 2 patients (Cases 21 and 25) in whom hypopotassemia and metabolic alkalosis followed major surgery.[29] They exhibited potassium and phosphorus loss in excess of nitrogen, retention of sodium relative to chloride, metabolic alkalosis, hypochloremia, changes in the electrocardiogram consistent with potassium deficiency as early as the first postoperative day, a fall in serum potassium concentration beginning on the third postoperative day, a fall in the eosinophil count to 0, hyperglycemia, glycosuria and a striking rise in the excretion of reducing steroids and ketosteroids.

Increased ketosteroid and "S" hormone* excretion in the urine is indicative of increased adrenocortical function.[65] Venning and her associates[66] have shown increased excretion of urinary corticoids after surgical trauma, and Forbes et al.[67] demonstrated increased ketosteroid excretion during the first few days postoperatively.

Reduction of circulating eosinophils is taken as evidence of increased adrenocorticoid secretion. Forsham and his co-workers[68] have used the fall in eosinophil count as a test of adrenocortical re-

*"S" hormone (sugar hormone) refers to the group of adrenocortical hormones responsible for gluconeogenesis and similar to "corticoids," "reducing steroids," Kendall's Compound E or Cortisone.

sponse to stimulation by ACTH, and Roche et al.[69] found that the eosinophil count fell to 0 or near 0 in 42 of 43 patients after operation.

Postoperative glycosuria and hyperglycemia offer further evidence of adrenocortical hyperfunction. Thomsen[70] observed spontaneous alimentary hyperglycemia or glycosuria in 63 per cent of 144 nondiabetic patients after trauma. Postoperative glycosuria has been reported by Albright.[50, 51] The insulin-resistant alimentary hyperglycemia of Cushing's syndrome is well known,[65] and glycosuria in normal persons has been produced by the injection of ACTH.[71]

We believe, therefore, that surgical trauma causes increased production of ACTH by the pituitary body, which stimulates the adrenal cortex to secrete one or more hormones ("alarm reaction"[72]). This reaction probably results in renal loss of potassium and loss or retention of chloride, but with retention of sodium relative to chloride, and development of metabolic alkalosis if there is inadequate provision of potassium postoperatively.

The extent to which adrenal hyperfunction may have contributed to potassium deficit in the cases observed cannot be assessed accurately with the present evidence. However, the development of adrenal hyperfunction following surgical trauma is well established, and there is a striking resemblance between the metabolic changes seen postoperatively and those associated with adrenal hyperfunction.

These statements imply that the events described are very likely to occur after any type of tissue injury — namely, surgical or accidental trauma, myocardial infarction, acute infections, radiation, nitrogen mustard therapy and so forth. Maintenance of an adequate potassium intake in these cases seems to be indicated.

Death from Potassium Deficit

The possibility of death from respiratory paralysis as a result of extracellular potassium deficit during recovery from diabetic acidosis has been emphasized in a number of reports.[42, 73-75] No cases of respiratory paralysis were observed in the patients reported here, but shallow, infrequent respirations were noted several days prior to death in the postoperative case described by Brunschwig[6] and in Case 20, who recovered on potassium therapy.

Animals made potassium deficient by synthetic diets or desoxycorticosterone may die, presumably of cardiac lesions.[46] The myocardial lesions consist of loss of striation, focal necrosis and leukocytic infiltration.[76-78] Potassium-deficient animals also show electrocardiographic changes similar to those in the potassium-deficient human being.[47] Myocardial lesions similar to those found in animals have been described in 2 patients whose deaths were attributed to potassium deficit.[78a, 78b] The development of frequent ventricular premature beats in several patients (Tables 3 and 4) suggests that ventricular fibrillation may eventually result if the deficit is not corrected.

Ileus resulting from potassium deficit may be a factor in postoperative death by contributing to fluid and electrolyte depletion and to malnutrition. A patient already critically ill may be brought to a needless operation for relief of obstruction (Case 3).

Prompt and adequate administration of potassium can easily prevent death from any of these causes.

A possible relation of potassium deficit to poor wound healing and disruption has already been discussed.

Phosphorus Deficit

Observations of low serum phosphorus levels (below 2.5 mg. per 100 cc.) in several cases (Table 1) indicate a definite parallelism with changes in serum potassium. Balance studies on 2 patients who were fed entirely by vein have shown the development of tissue phosphorus deficit postoperatively.[29] The clinical implications of this deficit are not yet clear, but the postoperative occurrence of increased glycosuria and hyperglycemia in these 2 patients, described above, suggests impairment of phosphorylating mechanisms. There seems to be a definite indication for provision of phosphorus along with potassium.

Therapy

Death after injudicious administration of potassium has been reported.[10] Cardiac arrest from heart block may occur in the human being at serum levels of about 10 milliequiv. per liter.[79-81] Potassium therapy should therefore only be undertaken with an understanding of the requirements, safe methods of administration and contraindications. Bodansky[82] has recently presented a comprehensive review of the conditions under which potassium toxicity may develop.

Measurements of the potassium balance during the early postoperative period in patients who are receiving no potassium indicate that daily urinary losses in excess of nitrogen may vary from 15 to 34 milliequiv. after relatively atraumatic operations such as herniorrhaphies and cholecystectomies.[11, 39, 40] After more traumatic procedures, such as pancreatectomy, gastrectomy, abdominoperineal resection and hypophysectomy, the daily losses of potassium tend to be substantially greater, but vary from 19 to 110 milliequiv.[29, 39, 48, 49]

Daily parenteral administration of 50 milliequiv. of potassium after relatively atraumatic procedures prevents potassium depletion in patients being maintained on intravenous administration of fluids.[11] After more traumatic procedures, the daily requirement can usually be met by the provision of 80 to 100 milliequiv. This amount is ordinarily adequate for repair of deficits also, since urinary losses tend to decline as the deficit grows.[29] Replacement

of potassium losses in most gastrointestinal fluids can be estimated adequately on the basis of 10 milliequiv. per liter of fluid lost.

Since urinary potassium losses are greatest during the first few postoperative days, early provision of potassium is indicated in patients who cannot eat and who must be fed parenterally. It should, however, be withheld during the first twenty-four to forty-eight hours postoperatively and from patients who are extremely dehydrated, whose urinary output does not exceed 500 cc. per day or who demonstrate nitrogen retention, unless the serum potassium concentration is low. Case 1, in which the serum potassium level rose transiently to 12.4 milliequiv. per liter on the first postoperative day, illustrates the danger that would have arisen from administering potassium within forty-eight hours of operation. The elevated level in this patient might be attributed to operative trauma, to the administration at operation of 4000 cc. of citrated bank blood, the plasma potassium level of which rises with the time of storage, and to postoperative dehydration and oliguria, which prevented excretion of the potassium.

The following forms of oral and parenteral potassium are used at this hospital: capsules of potassium chloride, 1 gm. every four hours (80 milliequiv. per day), which are taken with ample water or fruit juice; a mixture of potassium salts for oral use, which is recommended by Randall and his co-workers,[11] and is perhaps less likely to produce gastric distress*; and potassium chloride ampoules, each containing 1.49 gm. (20 milliequiv.) in 10 cc. of water, which can be added to glucose or saline solutions for parenteral administration in any desired quantity at the bedside. Two ampoules of potassium chloride per liter, providing a concentration of 40 milliequiv. per liter, are usually recommended. This can be administered safely at a rate of 80 to 100 drops per minute. In the presence of serious complications from potassium deficit, a concentration of 80 milliequiv. can be used. We have administered up to 160 milliequiv. (11.9 gm.) in one day without ill effect. Buffered potassium phosphate† (80 milliequiv. per day) was given parenterally with success in 2 patients[29] and may be preferable to the chloride because it replaces intracellular phosphate ion.

The use of the electrocardiogram as a guide to judicious potassium repletion has been emphasized,[10] particularly if determinations of serum potassium levels are not readily available. Return of flattened T waves and low ST segments to normal indicates adequate therapy, whereas the appearance of high, spiked T waves is the first indication of potassium toxicity.[10, 81, 82]

*4 gm. each of potassium acetate, bicarbonate and citrate are made up to 100 cc. with water; 15 cc. of this solution taken four times daily in water or fruit juice provides 71 milliequiv. of potassium.

†Each ampoule contains K_2HPO_4 (1.55 gm.) and KH_2PO_4 (0.30 gm.) in 10 cc. of water, providing 20 milliequiv. of potassium and 0.342 gm. of phosphorus.

Gamble[54] and others[11, 40, 88] have aptly emphasized the modest quantities of sodium chloride (2 to 4 gm.) and water (1500 to 2000 cc. as 5 to 10 per cent glucose) that meet the basic daily requirements of the adult patient on parenteral feedings. The dangers of exceeding these requirements, with due allowance for losses of fluids and sweat, have been stressed. Optimal parenteral electrolyte and fluid therapy can only be achieved by judicious provision of sodium chloride and water as well as the intracellular ion, potassium, and probably phosphate.

The average diet contains ample potassium as well as other obviously desirable nutritional components. Early feeding postoperatively is therefore vastly preferable to parenteral administration of fluids if the patient's condition allows it.

In this hospital the routine provision of potassium postoperatively to the patient who is not eating appears to have lessened appreciably the incidence of potassium deficit and the syndrome associated with it. It should be emphasized, however, that potassium deficit is not confined to the postoperative patient, but may occur before operation or in the nonsurgical patient, if the food intake is low or if there has been loss of gastrointestinal fluids, excessive administration of parenteral fluids, or tissue injury. Parenteral alimentation of the preoperative or nonsurgical patient should therefore include potassium, and probably phosphate, subject to the precautions stated above.

Summary and Conclusions

A syndrome occurring in patients after operation is described. It is characterized by clinical manifestations of apathy, lethargy, nervousness and irritability, muscular weakness, abdominal distention and occasional ileus, occasional confusion, disorientation, delirium, muscular twitching and tetany, electrocardiographic changes and occasional arrhythmias and edema; by blood chemical findings of hypopotassemia, metabolic alkalosis, hypochloremia, hypoproteinemia and, often, hypophosphatemia; and by a prompt reversal of the clinical and blood chemical abnormalities upon administration of adequate amounts of potassium.

The syndrome developed primarily in patients who were being fed parenterally and who received little or no potassium. Intracellular potassium deficit was demonstrated by balance studies on patients in whom the syndrome developed after operation. The deficit arises as a result of renal loss. Losses of potassium from intestinal fluids have been small or absent in most cases.

Simultaneous radiosodium and bromide spaces have shown an excess of sodium over the amount of chloride usually associated with it in extracellular fluid, and a tremendous increment in intracellular sodium, which probably replaces cell potassium. The excess of extracellular sodium over chloride determines the observed alkalosis.

Diminished erythrocyte potassium and increased erythrocyte sodium concentrations were found in several patients after development of the syndrome. Loss of intracellular phosphorus was also demonstrated.

Known factors in the pathogenesis of postoperative potassium loss are potassium deprivation, loss of gastrointestinal secretions, large infusions of glucose or saline solution, dehydration and malnutrition. These factors do not adequately account for some of the potassium losses observed.

Evidence is presented that adrenal hyperfunction resulting from surgical trauma leads to potassium deficit: the clinical and electrolyte disturbances seen in the syndrome resemble those described in some cases of Cushing's syndrome; metabolic alkalosis and potassium deficit have been produced frequently in human beings by the injection of adrenocorticotrophic hormone (ACTH) and Cortisone (Compound E); and there is a striking resemblance between other metabolic changes seen postoperatively and those associated with adrenal hyperfunction.

The suggestion is made that adrenal hyperfunction resulting in potassium deficit may occur after any type of tissue injury.

Prevention of the syndrome by provision of potassium early in the postoperative period is stressed. The various means of administering potassium and contraindications for its use are enumerated. The provision of phosphate ion seems also to be indicated.

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NEEDS IN THE FIELD OF PSYCHOLOGIC APPRAISAL OF CHILDREN WITH CEREBRAL PALSY*

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THE basic need in the field of psychologic appraisal in cerebral palsy seems to me to be the development of a simple test or group of tests that can be used by the average psychologist or physician to determine whether a child with cerebral palsy has the ability to achieve some measure of normal mental and emotional status in adulthood. To develop a need like this obviously is not simple since many aspects of cerebral palsy are not yet clarified even in the minds of persons working exclusively in this field.

For instance, there is still little correlation between causes, the physiology and pathology of cerebral palsy.[1] An uncommonly high regard for the I.Q. of the child rather than for his degree of over-all adaptability is still maintained although the latter is a more realistic concept of mentality. Scant attention is still paid to the relation of learning ability and the specific learning disabilities characteristic of these patients.[3] There is still resistance to the concept that cerebral palsy is merely one component of a group including convulsive disorders, mental deficiency and behavior disorders of organic origin.[3] It seems logical, therefore, to describe a practical method of over-all evaluation that has been used at the Meeting Street School for Cerebral Palsied Children in Providence, Rhode Island, during the past three years.[4] Here an effort has been made to develop a technic of evaluation of mental and emotional status based on the concepts of understanding and evaluation of the total behavior of the child with cerebral palsy.

The Meeting Street School is a day school to which these children are referred by local physicians for diagnostic evaluation, treatment, training and social experience. The morning sessions are devoted to the infant and nursery-school groups, and in the afternoon sessions, older, preadolescent children acquire group experience through instruction and guidance by the staff, composed of a director, nursery-school teacher, physical therapist, occupational therapist, speech therapist and psychologist. Medical guidance comes primarily from a pediatrician, who utilizes a host of specialists in the proper physical evaluation of the child.

Emphasis in the school program is placed on individual needs preferably through group experience, and many of the therapeutic technics for the individual are carried out while he is in the group. Parent education pointed toward the need for acceptance is considered an essential part of treatment.

It was soon discovered that if the school was to be successful, a policy must be defined that would limit the number of children to those who could be expected to achieve some measure of success in life. A decision was made to utilize psychologic examinations as a core around which medical examinations and staff observations could be integrated. This decision was reached after a few staff conferences on the definition of educability. After the staff had become familiar with the personality of these patients, the evidence was convincing that I.Q.'s should not be the only selective measure. This seemed logical especially since in early life psychologic examinations are not outstandingly reliable even for normal children.

PSYCHOLOGIC EVALUATION FROM THE MEDICAL EXAMINATION

Several leads to proper psychologic evaluation can be obtained from the history, physical examination and developmental status. These leads are based on clinical data accruing from research in cerebral palsy. The following items, for instance, are particularly helpful: congenital cerebral defects, a small number of which are genetically determined,

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are responsible for the majority of cases of cerebral palsy with severe mental deficiency (the mental status is higher in those whose brain injury is due to obstetric trauma[5, 6]); the incidence of mental deficiency is higher in children with paralysis of the right side than in those with left-sided disabilities, the cause of the latter being outstandingly traumatic in origin[7]; and children with heads of smaller than normal size are more apt to be retarded.[8]

Utilizing these premises when taking a history, I should guess that an Rh kernicterus baby was probably potentially more educable than a child whose brother was a convulsive and whose cousin could never sit, walk or talk. Similarly, I should guess that an infant with left-sided hemiplegia, probably as the result of a difficult mid-forceps delivery, was potentially smarter than a diplegic child whose mother had an uneventful pregnancy and delivery and who insisted she was a perfect baby until she had her first convulsion at four months of age.

As I examine such patients I tend to classify those who are "in contact" with the examiner as those who are most likely to succeed in any therapeutic program. The severely retarded child may be unaware of, disinterested in or unmanageable during the examination, whereas the intelligent child, regardless of the severity of his neuromotor handicaps, can frequently demonstrate his capacity somehow and is worthy of detailed follow-up studies, since a basic psychologic concept is that "intelligence will out despite disability." Likewise, although a history or evidence of delayed development in general cannot be used as a criterion for intelligence in the child with cerebral palsy, Holden,[9] the psychologist at the Meeting Street School, has statistical evidence that delay in speaking two or three word sentences after the age of thirty months correlates with a classification below the borderline level of intelligence. This is particularly appropriate in the evaluation of a child who has only a moderate disability and yet at three years can say only "Dada."

Just as one determines potential intelligence from history or neurologic status, there are several concepts about perceptual, behavioral and emotional difficulties that, if obtained from the medical history, are of aid in the psychologic evaluation. In the first place many children with brain injuries reveal characteristic disorders in form perception.[10] Secondly, the behavior of a child with a history of anoxia is frequently characterized by hyperactivity, poor attention span, distractibility and so forth.[11] And, finally, children, regardless of mentality, function at a lower level of intelligence when they are emotionally upset than when they live in a happy environmental climate.[12]

A typical patient in this category is an eight-year-old boy with minimal but definite signs of cerebral palsy, such as a strabismus, hyperactive deep reflexes and slight facial paralysis. His mother was upset because he was not permitted to go to school. The history reveals that he was a premature infant who required oxygen at birth. He presented a difficult feeding problem, and in addition his development was slower than normal, which was properly believed to be the result of prematurity. As a pre-school child he seemed as alert as his playmates, but was always overly active and had frequent temper tantrums. He had 3 siblings whom his mother never had trouble with but she could not handle the patient. She was impatient for the day when he would go to school — "perhaps the teacher would get him to relax." Since school, there had been nothing but trouble for all concerned. The teacher reported that she could not understand the boy. He appeared bright when she talked with him, but he seemed unable to learn anything; in addition, his behavior was incomprehensible. He was sweet as a teacher's pet one moment, and then suddenly — as if he was possessed — he was cantering about the room like a colt of *Man O'War*. The teacher's comment was "Sorry — but we just can't teach him a thing if he won't sit still."

The history, the utilization of cards demonstrating perceptual difficulties and the drawing of a man quickly revealed that this boy was educable. Psychologic procedures, including a Rorschach test, confirmed the clinical impression that this boy had a brain injury, with minimal neuromotor defects, and was functioning at a low intellectual level because of a specific perceptual difficulty and emotional disturbance. His behavior had so upset the family that he was being rejected, and this further interfered with the lower-than-average intellectual functioning. The understanding that such children also have cerebral palsy is important because they are much more common than those with severe neuromuscular disabilities, and they are much more salvagable — if properly evaluated and handled.

Evaluation from Psychologic Methods

After a proper medical evaluation, these children at the Meeting Street School are referred to the psychologist, who utilizes tests best suited to each child. The tests include the Revised Stanford-Binet,[13] Merrill Palmer Performance Scale,[14] Cornell Coxe Performance Scale,[15] Goodenough Test,[16] Rorschach Test,[17] the Thematic Apperception Test[18] and the Vineland Social Maturity Scale.[19] The special technics essential for maximal results from children with cerebral palsy depend upon skill and experience of the psychologist. Meyer and Simmel[20] describe an excellent approach that they utilize for children with neurologic defects at the Boston Children's Hospital. Using these standard tests with modifications when necessary, Holden[9] has found that 55 per cent of a group of 80 children tested were above the borderline range of intelli-

gence. Rather than place emphasis on I.Q., we stress the *range of ability* since that can be determined with a fair degree of accuracy and has more important implications than I.Q. in speech and occupational-therapy and physical-therapy situations. Naturally, these tests must be adapted to the handicap of the child if they are to be valid indicators of intellectual level.

Evaluation from the Nursery School

If the psychologic and medical evaluation are in accord, the child is accepted for observation in the nursery school, where the teachers, occupational therapist, physical therapist and speech therapist gain an impression of his assets and capabilities in individual and group contacts, since these therapies on the whole are carried out in a group setting. Since it is a policy always to have a few normal children attend the school for a few sessions, standards for comparison are always available. Progress in specific items is charted on a day-by-day or week-by-week basis. For instance, a girl, when first admitted, refused to join in group play, but sat in the sandbox and filled a pail in a repetitive manner. When substitution technics were carried out, she failed to respond. Similarly, the therapists could make little contact with her. After a month of this type of behavior she was discharged for treatment on a home basis because she was not regarded as educable. On the other hand, a boy admitted to the group in the same week soon left his solitary play to enjoy the group, and was accepted by them. Although he had little speech, the teachers discovered that children could understand and communicate with him. His acceptance into the group by the children and his willingness to participate was considered excellent corroborating evidence of normal mentality for his age.

Evaluation from Parent Interviews

The progress reports of parents are included in our method of psychologic appraisal. In cases in which parents report dramatic progress, not seen in the school, home visits are substituted. This technic is excellent not only for informational purposes but also because it serves to foster parent acceptance of the child in homes where tension has been accumulated in the care of a child with cerebral palsy. In almost every case in which we have helped the parents accept the child, there has been more rapid progress in therapy and adjustment, provided the child himself, of course, had capability that was not being demonstrated. In other words, emotional disturbance may additionally depress intellectual functioning already lowered because of earlier brain damage.

Final Evaluation

When the various impressions of the staff are recorded and reviewed, the correlation between formal psychologic tests, observational methods and medical evaluation was usually striking. In the few cases in which there was disagreement with the psychologic evaluation initially, after a one-year follow-up period, the staff finally agreed with the earlier psychologic findings.

Impressions

Our experience with this type of approach has left definite impressions regarding cerebral palsy that are worthy of mention. For all practical purposes, one must classify these patients as severely, moderately and minimally handicapped. Furthermore, we attempt to classify them as educable and noneducable. The latter group are a major problem. They are those who show no progress in any category in which they were adequately tested or tried. The parents of these children have our sympathy and understanding as well as our guidance in home or institutional care. However, we do not believe in expending large sums of money over long periods when there is scarcely any chance of their acquiring more than limited skills or any degree of social attainment.

The next major problem comprises the severely handicapped children whom we believe to have moderate intellectual capacity. Since it is obvious that these children will rarely ever become productive citizens, the greatest endeavors must be toward teaching them self-care and some way to achieve some enjoyment from life. A fourteen-year-old boy with severe athetosis can read, write poetry and play checkers with remarkable skill.

The moderately handicapped child of good intelligence will have a difficult time in gaining acceptance into the circle of normalcy in adult life, in spite of his innate abilities and acquired skills. Our major effort with this type goes into training in the jobs available to the handicapped adult. This child will require psychotherapy and guidance, since he will be hurt by the world about him.

The minimally handicapped child is perhaps the most challenging problem. He may grow up without any or only a few discernible handicaps, and yet his personality and learning abilities will be typical of the child with a brain injury, with, for example, hyperactivity, irritability or poor visual-form perception. Here every effort must be made to attain a careful evaluation of intellectual status and capabilities, since with proper education and guidance, these patients will be accepted into adult life and can become productive citizens.

Summary

The basic need in the psychologic evaluation of the child with cerebral palsy is the development of simple measures that can indicate educability and prognosticate the ultimate level of intellectual attainment.

A team approach to this need, in that the medical history and examination, formal psychologic tests and observational technics by teachers and parents all have equal status in the analysis of the whole child, is presented.

In the total evaluation, emotional factors when present must be considered, in addition to the more basic damaging effects of brain injury. Before an optimum functioning level can be reached, the aberrant behavior symptoms of the child and the rejecting attitude of the parents must be corrected.

Brain damage, in most cases, is the primary consideration of retardation in cerebral palsy, and at the present state of knowledge is irreversible for all practical purposes.

In general, it has been found at the Meeting Street School that although staff members may have disagreed with psychologic-test findings initially, after extended observations of the child socially, developmentally and adaptively, agreement has been reached with the earlier determined results of the psychologic examination.

Experience has taught that one is more apt to help a minimally handicapped child achieve a nearer measure of normal life than the severely handicapped. Although this realization does not minimize the demand for more accurate evaluation of the severely handicapped, it emphasizes even more the need for better understanding of the requirements of the minimally handicapped, since they are most apt to show the effect of proper training methods and educational technics.

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MID-CENTURY TRENDS IN CESAREAN SECTION*

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IN THE middle of the twentieth century, it seems fitting to review the status of cesarean section and some of the newer trends concerning it. Its use and abuse have covered pages of medical periodicals for the last twenty-five years.

From the reports from clinics all over the country, it is evident that there has been a gradual, upward trend in the incidence of cesarean section during the last fifteen years. During the same period maternal mortality has definitely decreased, until one wonders if in the next twenty-five years all operative obstetric procedures except low-forceps delivery will consist of cesarean sections. The more careful selection of anesthesia, the preparation and treatment of the patient with antibiotics and the more general use of blood transfusions have all helped to reduce the maternal and infant mortality and morbidity and have made cesarean section a safer procedure.

Another trend that is obvious, is that cesarean section, to a great extent, is replacing other operative obstetric procedures. High-forceps operations and craniotomies are a thing of the past. In a study of records for the last fifteen years, it is found that even with the increase in the incidence of cesarean section, the percentage of all operative procedures has remained practically the same. Therefore, sections must have reduced the number of difficult vaginal deliveries, which caused so much trauma to both mothers and infants.

Necessarily, the increase in cesarean sections has been due to some broadening of justifiable indications. In all reviews in the literature, cephalopelvic disproportion accounts for the largest number of sections. X-ray pelvimetry is being utilized more frequently in the primipara than formerly, and is helping to demonstrate the adequacy of the questionable pelvis. Especially is this true in the cases in which mid-pelvic disproportion is reported. With the protection of the antibiotics, it is now possible to give all borderline cases a better trial of labor because it is the character of the labor, itself, that often determines whether or not delivery through the vagina is possible.

The second most common indication is a previous cesarean section. Naturally, as the incidence of operations rises, the number of repeat sections also increases. There has been considerable discussion in the past few years of the feasibility of allowing patients to deliver through the vagina, if the first cesarean section was done for some other reason than cephalopelvic disproportion and also if the convalescence was afebrile. However, since about 30 to 40 per cent of primary sections are done for disproportion and in many cases it is not possible to obtain an accurate account of the previous operation or postoperative course, few patients are available for trial vaginal delivery. With the increasing safety of cesarean section, many obstetricians believe that it is not worth while to risk the possibility of a ruptured uterus and that the concept "once a Cesarean always a Cesarean" is a good one to follow.

Placenta praevia is the indication for the next largest group to be treated by cesarean section. The percentage done for this reason in all reviews has increased more than any other single indication. Because both maternal and infant mortality is decreasing greatly by this method, all patients but those who can be delivered by rupture of the membranes alone are delivered by section in most clinics.

Uterine inertia and cervical dystocia have shown a slight increase as indications. This is probably because manual dilatation of the cervix has been thrown into the discard, and again with the protection of the antibiotics, section is a safe procedure, even after several hours of labor.

Breech presentations and pre-eclampsia, as well as abnormal presentations, have shown a slight increase as indications. In the cases of pre-eclampsia, especially in primiparas, that do not respond to treatment and the termination of pregnancy is indicated, cesarean section is becoming the method of choice, particularly in the interests of the infant.

Premature separation of a normally implanted placenta accounts for a fairly stationary number of sections. Even in the absence of a fetal heart beat, it is often necessary to do a cesarean section in the interests of the mother.

Cardiac disease, as a primary indication for section, has markedly decreased.

The advent of knowledge of the Rh factor has necessarily broadened all indications to some extent. With the combination of an Rh– mother and an Rh+ father, one can never be sure whether the mother will not become sensitized in the first pregnancy, so that in a subsequent pregnancy the fetus might be affected. However, in cases that show antibodies, cesarean section because of possible erythroblastosis does not seem to be a justifiable indication per se because of the questionable prognosis for the infant.

The four types of section done most commonly in the United States are: classic; low flap, with either

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the transverse or the vertical incision; extraperitoneal; and cesarean hysterectomy.

The classic section is reserved for cases in which rapid delivery is imperative, for placenta praevia or for disease in the lower uterine segment. The low-flap operation seems to be the one of choice, and since 1940 the incidence of this method has progressively increased. All obstetricians are aware of its advantages over the classic section. During the last few years, the extraperitoneal approach has become popular. In some clinics it is done routinely in all cases in which the patients have been in labor for twenty-four hours or have had ruptured membranes for twelve hours or more. This operation has provoked much discussion, since many obstetricians believe that the same results may be obtained in potentially infected cases with the low-flap operation and the antibiotics. The low-flap section is simpler to perform, causes no injury to adjacent structures and does not require protracted wound drainage. The most common indications for cesarean hysterectomy are fibroids, uterine hemorrhages, infection and rupture of the uterus.

From the ward service at the New England Hospital for Women and Children, I have analyzed the figures on cesarean section for two different five-year periods to see if some of these trends are evident. The first period was from January 1, 1935, to January 1, 1940, before the advent of penicillin or the sulfonamides. The second period was from January 1, 1945, to January 1, 1950.

In the first period there were 3109 ward deliveries, with 82 sections, or an incidence of 2.6 per cent. In the second period there were 3181 deliveries with 138 sections or an incidence of 4.3 per cent, showing an increase of 1.7 per cent. There were 2 maternal deaths in the first series, giving a mortality of 2.4 per cent. There were no deaths in the second series.

The first death occurred in 1937. The indication for cesarean section was placenta praevia. The patient bled profusely before and during the operation. A classic section was done, and the patient died four hours later. At that time there was no blood bank in the hospital, and to obtain blood from a donor and give it to the patient seemed to be a major operation. The record states that the patient had not yet received 500 cc. of blood when she died. With present-day methods of treatment and plenty of blood on hand this death would probably have been avoided.

The second death also occurred in 1937. The patient was a twenty-six-year-old primipara with rheumatic heart disease. She was admitted ten days prior to operation with cardiac failure. She was digitalized, and when her condition seemed satisfactory, a classic cesarean section with sterilization was done under local anesthesia. The baby weighed 3 pounds, 7 ounces. The patient had a very stormy convalescence, and on the tenth day she became very distended and developed a paralytic ileus. On the eleventh day the abdominal incision opened, eviscerating the small intestine. She died on the following day. With present-day concepts of the treatment of pregnancy in rheumatic heart disease, this death also might have been avoided.

The morbidity rate was 44.5 per cent in the first series and 31 per cent in the second series with the addition of antibiotics. The incidence of difficult mid-forceps delivery was 5.8 per cent in the first and 3.2 per cent in the second series. Thus, traumatizing operative procedures were reduced.

Cephalopelvic disproportion as an indication was practically the same in both series, being 35.4 per cent in the first and 36.7 per cent in the second. Twenty-nine per cent of cases were done in the first series as repeat sections, and 31 per cent in the second series. Placenta praevia was the indication that showed the greatest increase. In the first series 6 per cent and in the second series 12 per cent of operations were done for this reason.

In the first series there were 18 classic and 58 low-flap operations; there were 5 cesarean hysterectomies. In the second series, there were 26 classic sections, 111 low-flap operations and 1 extraperitoneal section; there were no cesarean hysterectomies in this series. In the first series, the indications for cesarean hysterectomies were as follows: fibromyoma, 2 cases; abruptio placentae, 1 case; adenocarcinoma of the cervix, 1 case; and sepsis of the uterus, 1 case. The patient had been in labor for seventy-two hours and had had ruptured membranes for sixty hours. She had a chill and elevation of temperature prior to operation. She had an uneventful convalescence.

In the second series, the extraperitoneal section was done on a patient in whom cephalopelvic disproportion was undiagnosed. She had been in labor for fifty hours and had had ruptured membranes for thirty-six hours.

The management and treatment of cesarean section on the ward service begins in the Prenatal Clinic. All primiparas and multiparas with previous dystocia are seen during their last month of pregnancy by the attending obstetricians to try to determine the best possible type of delivery. X-ray pelvimetry is done on all patients who present the following conditions: contracted pelvis, primipara with unengagement of the fetal head, multipara with a previous history of dystocia and abnormal presentations. Trial labors are allowed in all borderline cases. Three hundred thousand units of penicillin is given every twelve hours in all trial labors and in elective cesarean sections when rupture of the

membranes precedes the operation. All patients are cross-matched preoperatively, and blood is available in the operating room. The low-flap operation with a transverse incision has been the operation of choice. Repeat sections are done on all patients having previous operations. The minimal amount of preanesthetic medication has been used. Cyclopropane or spinal anesthesia has been used in the majority of cases. All patients are permitted out of bed in twenty-four hours.

Summary

With the increase in the incidence of cesarean section in the last fifteen years, there has been a decrease in other obstetric operative procedures.

There has been a general trend to broaden the indications for cesarean section.

With the protection of the antibiotics, there has been a decrease in maternal mortality and morbidity.

MEDICAL PROGRESS

TUBERCULOSIS

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The Problem

OUT of the maze of material on tuberculosis the following subjects have been selected for discussion in this report of progress.

The tuberculosis problem in 1950 as compared with 1900.

The present emphasis on the discovery of early cases, particularly by mass x-ray surveys of "healthy" persons. What are the results of these surveys to date, and are they really worth while?

When is a tuberculous lesion, as shown in the x-ray film, to be regarded as active? What has been accomplished in deciding this point by culturing the sputum and gastric contents for tubercle bacilli? What is the present status of laboratory studies of the blood serum to determine the activity of a given tuberculous process?

Just how valuable is the antibiotic treatment of tuberculosis, and what is the relative value of streptomycin, dihydrostreptomycin, para-aminosalicylic acid, tibione and other substances that have been tried?

What is the present status of the surgery of pulmonary tuberculosis? Is thoracoplasty holding its own as the surgical treatment of choice? When should surgical excision be used? Do the results of decortication of lungs bound down by partially organized pleural exudate justify this procedure?

How extensively should BCG vaccination be used in the United States as a means of "stamping out tuberculosis"? Should a campaign to "immunize" all persons who have a negative tuberculin test be started?

The aim of this report is to present a summary of the most helpful articles bearing on these points, and then to give a summary of my conclusions about where medicine stands today on these problems. The literature covered is largely that published in the year 1949 and the first half of the year 1950.

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The Evidence

1900 vs. 1950

At the half-way mark of the century there is a certain fascination in comparing the present status of the tuberculosis problem with that of 1900. At the beginning of the century the death rate from all forms of tuberculosis for the United States registration area was 202 per 100,000 population; in 1948 it had dropped to 30. In Massachusetts the rate in 1900 was 253, and in 1948 it was 29.6.

In 1900 tuberculosis headed the list of all causes of death. In 1946, at a time when the average life span was being extended, infections of all sorts were under better control, and the degenerative diseases were coming to the fore, tuberculosis stood seventh in the list, with the numerically more important causes of death and their rates as presented in Table 1.[1]

In spite of the fact that, when deaths at all ages are considered, tuberculosis seems less significant than before it should be remembered that it is still the leading cause of death among persons who die between the ages of fifteen and thirty-five. However, the age at which death from tuberculosis occurs is steadily advancing. In 1900, 64 per cent of all the reported deaths from tuberculosis took place in the group from fifteen to forty-four years of age, whereas in 1947 only 45 per cent of the deaths from tuberculosis were between those ages.[2] Even with a steadily falling death rate about 1000 Americans are still dying each week from tuberculosis, and about 500,000 living Americans have active pulmonary tuberculosis.[3]

By 1900 Dr. Trudeau had proved the value of rest and sanatorium care, the "Adirondack Cottage Sanatorium" was well established at Saranac Lake, and the first tuberculosis institution supported by public funds had been established at Rutland in 1898 by the Commonwealth of Massachusetts. The discovery of the tubercle bacillus had opened up many possible animal experiments for the cure of tuberculosis, but Koch's tuberculin and other measures had given only discouraging results. "Rest, fresh air and good food" was the formula for treatment. It is still a good formula, but much that is new and helpful had been added by 1950.

TABLE 1. *Leading Causes of Death in 1946.*

CAUSE OF DEATH	DEATH RATE PER 100,000 POPULATION
1. Diseases of heart	307
2. Cancer	130
3. Intracranial lesions of vascular origin	90
4. Accidental deaths	70
5. Nephritis	58
6. Pneumonia and "influenza"	45
7. Tuberculosis	36

Before a report of "progress" during the past year it is of interest to compare death rates in the United States with those of other countries (Table 2). There is no doubt that many public-health authorities would give credit for the low death rate in Denmark to the widespread BCG inoculation now practiced in that country, but it will be noted that the rate is essentially the same as that of the United States, where very little BCG is used.

Mass Surveys to Discover Early Cases

Since 1900 there has been a growing effort to find, isolate and treat the early and often asymptomatic case. The first groups studied were school children because of the belief that the disease usually started early in life and if treated during childhood would not become active later. Then followed examination of the special group with industrial hazards such as silica, the group of contacts with known open cases and, finally, the "mass x-ray surveys" of the supposedly well. Such a search for unknown active cases is of importance because it is estimated that only half the 500,000 active cases in the United States are known to the health authorities today.[3]

The important details about the conduct of such a study are very well recorded by Zacks,[8] chief of clinics, Massachusetts Department of Public Health, and he has written a special article[9] stressing the fact that, "Pre-survey planning should go far beyond the mass x-ray procedure itself and include arrangements for final diagnosis and care of discovered cases." It is estimated that, in 1949, 14,000,000 small survey chest films were taken in the United States.[10]

The number of previously unknown and finally proved active cases of pulmonary tuberculosis discovered by this method is small in comparison with the total number of persons examined. In Baltimore it was 7/100 of 1 per cent, in Seattle, 1/10 of 1 per cent, and in Washington, D. C., 15/100 of 1 per cent.[10]

The preliminary figures for the recent Boston "Chest X-Ray Program" concerned a total of 536,012 examined. Small films showed tuberculosis in 4003 and suspected tuberculosis in 4067 cases. Large films showed tuberculosis in 4122 and suspected tuberculosis in 443 cases. Of 343,000 Boston residents examined 247 new active cases were discovered (7/100 of 1 per cent).

The final analysis of the Baltimore study is given by Silverman,[11] and the percentage of active cases discovered was exactly the same as that in Boston.

A review of statistics to date, then, shows that a mass city survey can be expected to reveal about 1 per cent tuberculosis suspects and 1/10 of 1 per cent of active disease.[12] A few years ago it was estimated that such surveys would disclose 1 per cent of active cases.

In England the National Association for the Prevention of Tuberculosis reports[13] that about 2,000,000 chest x-ray films are taken each year with a finding of active tuberculosis in 4/10 of 1 per cent.

TABLE 2. *Death Rates in Various Countries, 1945-1948.*

COUNTRY	YEAR	RATE PER 100,000 POPULATION
Japan	1945	280[4]
Turkey (Istanbul)	1947	267[5]
Greece	1948	250[6] (approximate)
Denmark	1947	30[7]

Very careful studies by Medlar, Spain and Holliday[14] have disclosed a "disregarded seedbed of tubercle bacilli." The study is based on autopsy records at the Bellevue Hospital, New York City, of all deaths occurring in patients over the age of fifteen. The authors conclude that tuberculosis acquired later in life tends to be less explosive, and the manifestations may be so few that patients do not seek a physician's advice. Nevertheless, they are dangerous spreaders of infection.

Another often unrecognized focus of tuberculosis is in institutions for those with mental disease. A recent survey[15] of seven such institutions in California disclosed a death rate of 600 per 100,000 resident population.

Cultures and Other Tests to Determine Activity

Cultures. For many years the only method of certainly establishing the diagnosis of pulmonary tuberculosis was by acid-fast stain of the direct smear of the sputum. In cases of doubt a guinea pig was

sometimes inoculated. In recent years "concentration" of the sputum by the use of alkaline solutions has become popular although many workers have maintained that smears made of *selected* sputum particles gave fully as large a percentage of positive results.[16] Where the direct smear or concentration methods fail the proper *culture* technic is proving to be as sensitive a method of demonstrating tubercle bacilli as animal inoculation and cheaper. Consequently, more and more laboratories are prepared to culture various specimens for tubercle bacilli. In this way a diagnosis hitherto only suspected may be once and for all established.

Cultures are now made of sputum, laryngeal swabs, tracheal specimens, bronchoscopic specimens or, finally, gastric contents. During the year several articles have appeared giving the percentage of positive cultures under different conditions, as well as articles that stress the importance of a positive culture in determining the treatment as well as the diagnosis of disease. It has been surprising how often the culture of the gastric contents, for instance, has been positive for tubercle bacilli when there has been no sputum or a negative sputum. This finding may be a great asset. But the rub comes in determining how much stress to place on an *occasional* positive culture in a patient who is clinically well. Sometimes one would prefer not to know what the culture might show. And some hospitals insist on so many consecutive negative cultures that it becomes very difficult to get the patient discharged.

Freiman and Pinner,[17] of the Montefiore Sanatorium, in a very careful study, report that cultures are at least two to five times as effective as microscopical methods.

Smith,[18] at the Barlow, California, Sanatorium, reports a program that includes the examination of two thirds to three fifths of *all* sputum expectorated during the first three months of residence, by concentration and culture and partly by animal inoculation. In addition, stomach contents were examined by culture and inoculation once each month. During a ten-year period positive bacteriologic results were obtained in 97.4 per cent of clinically active cases, resident two months or more, and in 94.6 per cent of clinically active *minimal* cases of tuberculosis. Such a program puts a great strain on the laboratory, but it shows what can be done.

In an exhibit at the recent meeting of the National Tuberculosis Association, Smith, Palmer and Bosworth went one step farther and showed that of 97 student nurses whose tuberculin tests had recently converted from negative to positive there were 15 who gave positive cultures of the stomach contents (checked by guinea-pig inoculation) and 8 of the 15 showed *no x-ray changes*.

Wardrip et al.,[19] of San Jose, California, report on the combined use of tracheal lavage and culture as a diagnostic procedure. They claim that in 199 patients with negative bacteriologic findings, by direct sputum examination, tubercle bacilli were cultured from specimens obtained by tracheal lavage in 111 cases. Gastric lavage in 86 of these 111 patients gave tubercle bacilli by culture in only 24. To obtain the tracheal specimen, 5 cc. of sterile distilled water is introduced into the trachea through a laryngeal cannula, and the patient coughs the washing into a sterile container. Occasionally, culture of a laryngeal swab will provide acid-fast bacilli when no sputum is available and the gastric contents are negative.[20]

So much for the diagnostic value of cultures. Now what is the prognostic significance of the positive culture, particularly the *occasional* positive culture of the gastric contents, in a patient clinically well? Chang,[21] of Rutland State Sanatorium, reported on 621 patients discharged after June, 1925, and found that almost twice as many with occasional positive cultures had recurrences as those with constantly negative cultures.

Likewise, Abeles,[22] of New York City, studied the records of 199 discharged patients and reported almost three times as many readmissions in the group with occasional positive cultures.

Other helpful laboratory suggestions are a rapid mouse test for laboratory diagnosis[23, 24] and the slide culture method of Pryce.[25, 26] By the mouse method tubercle bacilli were isolated from 14 patients ten to fifteen days after inoculation. By the slide culture method streptomycin sensitivity can *sometimes* be determined in a week. In a recent exhibit at the meeting of the National Tuberculosis Association Lowry and Berry, of Denver, demonstrated this method and claimed 82 per cent positive cultures as compared with 84 per cent on ordinary culture mediums. And their results were obtained in *two to six days*.

Other methods. Middlebrook and Dubos,[27] of the Rockefeller Institute, have developed a specific serum agglutination of erythrocytes sensitized with extracts of tubercle bacilli. Many investigators are trying this test, but the consensus at present is that this is not a test for clinical activity although the procedure is of immunologic interest. Dr. David Smith, of Duke University, gave this as his opinion when he reported at the meeting of the National Tuberculosis Association in April.

Other investigators have been interested in the fact that the serum gamma globulin is increased in patients with active tuberculosis[10, 28] and decreased in those with pulmonary carcinoma.

Favour and his co-workers[29, 30] at the Peter Bent Brigham Hospital in Boston have been studying the lysis of human white cells by tuberculoprotein. They find that the lymphocytes from tuberculous human beings are specifically sensitive to tuberculoprotein.

Leyva,[31, 32] of the Quezon Institute, Philippine Islands, describes a serum color reaction, using diphenylamine reagent, which was positive in 684 of 698 cases of active tuberculosis. He believes that the positive response is attributable to nucleic acid derived mostly from the tubercle bacilli.

Kahn[33] comments on a precipitation test with a lipid antigen that he thinks may be of value as an index of activity.

Antibiotics

Streptomycin. It was more than sixty years after the discovery of the tubercle bacillus that a drug was found that could successfully combat this organism under all three conditions in which it grows—namely, in the test tube, the laboratory animal and the human patient. But more than four years of experience has shown that streptomycin is a drug really effective in the struggle with tubercle bacilli, and a new era in the handling of tuberculosis has begun. The most startling result has been the "cure" of certain cases of proved tuberculous meningitis, a disease hitherto regarded as 100 per cent fatal. However, streptomycin is by no means a cure for all tuberculosis, particularly for chronic fibrocavernous disease. It gives the best results with an acute exudative process, but here also it should be accepted as only an adjunct to bed rest, collapse therapy or surgical measures. The early symptomatic and x-ray improvements are often striking, but sputum conversion is disappointingly low and relapses are frequent. As suggested by Hinshaw it acts like a fire extinguisher, putting out the flame of acute disease, but is apt to leave smoldering timbers that will usually require further medical or surgical attention if a future outbreak of fire is to be avoided.

The effective dosage and the toxic range have been well established. Under most conditions 1 gm. intramuscularly, once a day, is both effective and nontoxic, and there is little of the vertigo that was common with the original 2-gm. dose. There are, of course, exceptions. Continued high blood levels are not necessary. Intermittent therapy with one dose twice a week (or daily doses for short periods with rest periods between) is therapeutically effective. The duration of treatment, if the best results are to be obtained, should probably be as long as four months. But it was early discovered that after six weeks of treatment the tubercle bacillus was apt to become resistant to streptomycin, and until the past year many investigators have insisted on short periods of treatment, except for tuberculous meningitis, in which heroic dosage seemed necessary. Unfortunately, resistance develops most quickly in cases with definite cavity, in which prolonged treatment seems most necessary. The intermittent therapy mentioned above delays the emergence of resistance, and during the past year attention has been focused on the use of para-aminosalicylic acid (PAS) for this purpose. PAS is also of value if used alone. Most investigators agree that if cultures once show resistant organisms further treatment with streptomycin is useless and probably harmful. However, clinical observation does not always agree with this conclusion, and it has been shown that an individual patient may harbor both sensitive and resistant forms.

Most investigators have held the policy that streptomycin should not be given in cases in which older, tested methods promise a cure. The fear of the development of resistant organisms has been the main reason for withholding the drug. Consequently, streptomycin is rarely given for minimal, noncavernous disease even though it might, in these cases, be of the greatest help in effecting a permanent cure with the least danger of leading to resistant forms. The analogy used early in streptomycin argument that if a hunter has only one cartridge he should not use it to kill a skunk when there is a tiger in the offing does not apply because one is not dealing with a skunk and a tiger but with a playful young tiger who can be killed easily now but with much more difficulty if allowed to wander off into the jungle and grow up. Perhaps the effect of para-aminosalicylic acid on resistance will change the present point of view. Even as things are there is much to be said for the use of streptomycin in minimal tuberculosis in the adolescent girl in whom, with other methods, the outlook is at best uncertain.

Streptomycin is of great value in the treatment of extrapulmonary tuberculosis, such as laryngeal, bronchial, intestinal, genitourinary, pericardial, peritoneal, "glandular" and bone and joint disease, and in tuberculous sinuses. Sometimes, a short course of streptomycin is given for the relief of symptoms from these extrapulmonary foci without expectation of a cure.

An amazing amount of work is being done to evaluate the drug and determine how it is best used. The Veterans Administration, with the Army and Navy, the American Trudeau Society (Medical Section of the National Tuberculosis Association) and the United States Public Health Service are all extensively involved. Such a large amount of controlled study has never been given to one drug in so short a time.

The best short summaries of the results of streptomycin treatment of tuberculosis are those presented to the Council on Pharmacy and Chemistry of the American Medical Association by the Streptomycin Committee of the Veterans Administration, in association with the Army and Navy, in 1947,[34] 1948,[35] and 1950.[36] This work is also summarized and analyzed with great care by Tucker.[37] The studies sponsored by the American Trudeau Society are reported in full in book form by Riggins and Hinshaw[38] and summarized by them in a recent review.[39]

There are many possible sources of figures on the results of streptomycin treatment, but this article is confined largely to the statistics as given in the recent report from the Veterans Administration, Army and Navy.[36] The subject is very well summarized in a recent editorial.[40] These figures are based on reports from 42 hospitals, which have treated 7000 patients with all types of tuberculosis, by 22 different regimens, over a four-year period. The results are very sketchily shown in Table 3.

"End-result" figures are beginning to come in from the studies started four years ago. At the National Tuberculosis Association meeting in April, 1950, Dr. Canada reported the follow-up results, three years after completion of treatment, on the original 202 patients in the Veterans Administration, Army and Navy series. Their dosage was 2 gm. a day for one hundred and twenty days. Of the 202 patients 28 per cent are dead, and 37 per cent arrested, and 25 per cent relapsed after treatment was completed.

TABLE 3. *Results of Streptomycin Therapy of Pulmonary and Extrapulmonary Tuberculosis.*

RESULT	PERCENTAGE
Pulmonary lesions:	
X-ray improvement (marked or moderate) in 375 cases	66
Relapse during year after treatment	35
Mortality in 416 cases during 2½ yr.	21
Toxicity:	
Vertigo with 2 gm. for 120 days	80
Vertigo with 1 gm. for 60 days	30
Laboratory findings:	
Sputum conversion in pulmonary cases	32
Resistant organisms in cases with positive sputum after 42 days' treatment	40
Resistant organisms in cases with positive sputum after 120 days' treatment	75
Resistant organisms remaining in the entire series (negative and positive) after 120 days' treatment	51
Extrapulmonary lesions:	
Improvement in laryngeal, bronchial, intestinal and peritoneal tuberculosis and tuberculous sinuses	85
Genitourinary cases:	
Cystoscopic and symptomatic improvement	80
Improvement in renal destruction	20
Conversion in urine after 2 gm. for 120 days	85
Conversion persisting after 2 yr.	57

No actual figures are given for bone and joint tuberculosis, but in the summer of 1949 a "jury" of orthopedic surgeons reviewed the roentgenograms of 196 patients treated with streptomycin and concluded "that improvement occurred more rapidly and to a somewhat greater extent in patients who received streptomycin than in those who had no chemotherapy and that surgical procedures were made possible which would have been impossible without it."[36]

Special articles on the treatment of extrapulmonary lesions include reports on tuberculous enteritis,[41, 42] tuberculosis of the endometrium,[43, 44] tuberculous sinuses of vertebral origin[45] and bone and joint lesions in 300 French patients.[46]

Miliary and meningeal tuberculosis. It is in a way unfortunate that miliary and meningeal cases have often been combined in streptomycin tables because cures of miliary disease without meningitis did sometimes occur before streptomycin, whereas proved tuberculous meningitis has until now been considered 100 per cent fatal. A combination of the two still presents an almost hopeless outlook.

Relapses after the cessation of treatment are so frequent that conclusions about the final results cannot be drawn until patients have been observed for many months. Consequently, the best series from which to judge results are the first 100 cases of miliary and meningeal tuberculosis treated in the Veterans Administration study. It is now three years since treatment was stopped on these cases, and Dr. Paul Bunn has recently summarized the results.[47-49] The survivals in the 81 cases of meningitis, including those with accompanying miliary disease, numbered only 9. And of the nine, 4 had "serious residua" (deafness, blindness and paralysis). This leaves 5 "cures," or 6 per cent, and all these patients are still subject to relapse. With such a figure one cannot help wondering whether the streptomycin treatment of tuberculous meningitis, with its very prolonged, often painful, and always very expensive treatment, is at present truly "mandatory." However, it should be pointed out that when there is only meningitis without miliary disease 20 per cent of patients in the original series have so far survived. The survivals in the second 100 cases are not as many as in the first 100 reported above.

The early investigators all gave streptomycin both intramuscularly and intrathecally in cases of meningitis, but it was soon found that a dose larger than 50 mg. intrathecally was often irritating. Since streptomycin appears in effective levels in the spinal fluid after intramuscular injection if there is meningeal inflammation a number of investigators have given up intrathecal administration.

Because deaths occur for the most part from degenerative hydrocephalus, often with widespread cerebral arteritis and thrombosis or severe encephalitis, Cathie[50] has reported the use of streptokinase, and others have suggested the use of heparin.

The results in children are distinctly better and have usually been obtained when some other drug is given in addition to comparatively large doses of streptomycin. Lincoln and Kirmse,[51] of Bellevue Hospital, report on 21 cases of tuberculous meningitis treated with a combination of streptomycin and Promizole. Sixteen of the 21 patients still survive, 11 for twelve to twenty-seven months. In the other 5 cases the survival time is three to eleven months. Of the 16 patients there is deafness in 3 and muscle weakness in 3 others. The authors emphasize the fact that drug-resistant strains develop much less frequently in meningitis than in other forms of tuberculosis.

Data from foreign countries are about the same as those from the United States. In Paris[52] 17 of

100 patients with tuberculous meningitis are said to be well after two years. In England[53] 18 of 54 patients showed complete clinical recovery after eight months or more of observation. From Greece[54] comes a report on 63 cases of tuberculous meningitis in children, with 29 survivals. Fouquet et al.,[55] at the Salpêtrière Hospital in Paris, report meningitis in 147 children treated in the course of two years. Of those with meningitis alone, without miliary lesions, 33 per cent recovered. When sulfone was added to the streptomycin 59 per cent recovered. Nayrac and his associates,[56] of Paris, are now using intraventricular administration of streptomycin systematically in all cases.

Streptomycin-resistant tubercle bacilli. As already noted, the early emergence of resistance to streptomycin has been one of the troublesome factors in planning the effective use of the drug. Tucker[37] reports the cumulative rates for the emergence of tubercle bacilli resistant to 10 microgm. or more per cubic centimeter when streptomycin was administered daily as follows: first month, 20 per cent; six weeks, 35 per cent; second month, 50 per cent; third month, 62.5 per cent; and fourth month, 75 per cent.

"The development of resistance appeared to depend on the *duration* of treatment. . . The curves of incidence for 2.0, 1.0, and 0.5 gm. doses, given daily for 120 days, were practically identical."[38] So that the development of resistance seems to depend on the number of days in which treatment is given and not on the amount of drug or the number of times it is given during the day. Unfortunately, if one cuts the number of days of treatment from one hundred and twenty to forty-two there is an appreciable loss of therapeutic efficiency. However, if one interrupts treatment and gives 1 or 2 gm. every third day (or twice a week) for one hundred and twenty days, or daily treatment for four weeks, followed by a rest period of four to six weeks, and then repeats the course, the therapeutic effect is apparently as good as that with daily doses for the long period, and emergence of resistance is definitely delayed. This plan of treatment has been tried extensively at the Fitzsimons General Hospital of the Army.[57]

It is of interest and importance to try to determine if there are certain types of pulmonary tuberculosis in which resistant forms are more apt to appear, and it has been shown that this is true in cases with marked cavitation and caseation. Howlett et al.[58] found that in 33 of 56 patients with frank caseation or cavity, resistant forms developed in forty-two days, whereas they did not appear on any of 31 patients without such lesions. Similar results were obtained by Howard and his co-workers[59] and Mitchell.[60]

Howlett and O'Connor[61] point out the great value of streptomycin in disseminated nodular tuberculosis of a subacute or chronic type without definite caseation or cavity.

The articles dealing with the use of para-aminosalicylic acid to delay resistance are discussed below.

Reports from foreign countries. There is general agreement in all parts of the world concerning benefit of streptomycin. In England the Streptomycin in Tuberculosis Trials Committee of the Medical Research Council reports[62] on 107 patients with acute progressive bilateral pulmonary tuberculosis unsuitable for any treatment except bed rest. Fifty-two were continued on bed rest alone, and 55 were given 2 gm. of streptomycin daily for 6 months. At the end of this time 7 per cent of the patients treated with streptomycin had died, as compared with 27 per cent of the others. X-ray examination showed "considerable" improvement in 51 per cent of the streptomycin-treated cases and in only 8 per cent of the untreated. The percentage of deterioration was 18 in the streptomycin group and 34 in the others.

Streptomycin in pregnancy. Considerable interest has been shown in the possible harm to the fetus if streptomycin is given to a pregnant woman. So far no harm to the fetus has been shown,[63,64] and the mother has often been greatly benefited.

Streptomycin with collapse therapy. It is now agreed that in a given case early improvement with streptomycin should not blind one to the possibility of future relapses. Hence every advantage should be taken of the chance to start artificial pneumothorax or pneumoperitoneum or to perform operation at the optimum time. Hyman and Hoffman[65] report on 90 consecutive cases of pulmonary tuberculosis treated with streptomycin and pneumothorax. Seventy of the 90 (78 per cent) had excellent or good "final" results.

Dihydrostreptomycin. This modification of streptomycin was once widely heralded because it was said to be much less toxic than the original drug. Its special value is now doubted. The recent Veterans Administration report[36] summarizes the present opinion as follows:

> The data suggest that, in equivalent daily dose (e.g., 1.0 Gm.) dihydrostreptomycin is somewhat inferior to streptomycin in point of therapeutic efficacy and that, although when examined by caloric tests it has less effect on the function of the vestibular nerve, when it is given in the larger daily dose of 2.0 Gm. (and certainly when given in still larger doses) it may produce a loss of hearing during or even after the completion of treatment, which has rarely been observed with streptomycin. All in all, the investigators are dubious of the usefulness of dihydrostreptomycin and believe that as long as a daily dosage of 1.0 Gm. of streptomycin is considered adequate therapy the chief value of dihydrostreptomycin will be found in cases in which there is unusual susceptibility to the toxic manifestations of streptomycin or sensitivity phenomena.

A similar opinion is rendered by the Clinical Subcommittee of the Committee on Medical Research and Therapy of the American Trudeau Society.[66]

The *American Review of Tuberculosis* for November, 1948, contains six articles of dihydrostreptomycin, and the *New England Journal of Medicine* one on toxicity by Allison et al.[67] of the Rutland Heights Veterans Administration Hospital.

(To be concluded)

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 36401

PRESENTATION OF CASE

A forty-three-year-old woman entered the hospital because of pain in the low back and legs.

About nineteen years before admission, shortly after a minor pelvic operation, the patient gradually developed severe, dull, throbbing pain in the low midline back, both buttocks and throughout both legs. The pain was constant but was aggravated by lying down, straining, bending, coughing, sneezing, yawning and emotionally disturbing situations. Seventeen years before admission one ovary and one tube were removed, without relief. About three years after this operation she became relatively free of pain for about three years. Pain then recurred, persisted with varying intensity during the ensuing years and became increasingly severe in the year before entry. During this period she underwent psychoanalysis for two years, and a hysterectomy was performed. In the month before admission several attempts at lumbar puncture were made, but no fluid could be obtained. Throughout the course of the illness there had been no muscular weakness or impairment of co-ordination. The patient had had marked urinary frequency increasing during the months before admission but no incontinence, and just before admission she had been constipated. She occasionally had "numbness" in the feet and hands after exertion but had no loss of sensation. The general health had been fairly good although she was subject from time to time to bouts of diarrhea. She had had no significant loss of weight.

Physical examination showed a patient who appeared generally well. The heart, lungs and abdomen were normal. Forward bending of the spine was limited by low-back pain to 45°, and straight leg raising, similarly productive of low-back pain, was restricted to 60° on the right and 65° on the left. There was no tenderness of the spine, but pressure over the lumbar spine gave rise to pain in the buttocks. The cranial nerves were intact, and strength, co-ordination and sensation were normal in the arms. She used her legs well in walking and in tests of co-ordination, but there was a very slight degree of weakness in dorsiflexion of the feet and toes. The tendon reflexes were normally active and equal in the arms. The abdominal reflexes were normal. The right knee jerk was less active than the left, which was normally active. The ankle jerks were absent. The plantar reflexes were normal. Pain and light-touch sensation were very slightly impaired over both buttocks, including the midline, and down the posterior aspects of both thighs as far as the knees. Sensory findings elsewhere were normal.

The temperature was 98.6°F., the pulse 68, and the respirations 20. The blood pressure was 160 systolic, 80 diastolic.

The urine gave a +++ test for albumin and had a specific gravity of 1.014, and the sediment contained 16 red blood cells and 45 white blood cells per high-power field. The hemoglobin was 15.5 gm. per 100 cc.; the white-cell count and differential were normal. X-ray films of the lumbar spine showed thinning of the pedicles with widening of the interpedicular spaces from the second to the fourth lumbar vertebra, a sharply defined defect superiorly in the left lamina of the third lumbar vertebra and erosion of the posterior aspects of the bodies of the third and to a lesser extent of the second lumbar vertebra (Fig. 1 and 2).

FIGURE 1. *Anteroposterior View of the Lumbar Spine. Arrows indicate the increased interpedicular distance at the third lumbar vertebra, with thinning of the pedicles.*

On the fourth hospital day an operation was performed.

Differential Diagnosis

Dr. James C. White*: "Forward bending of the spine was limited by low-back pain to 45°, and straight leg raising, similarly productive of low-back pain, was restricted to 60° on the right and 65° on the left." Dr. Joseph Barr and I have tried straight leg raising on the operating table with the nerve roots exposed and found that the nerves moved in and out of the intervertebral foramen for almost a centimeter. If there is a lesion close to one of these caudal roots it is perfectly obvious that straight leg raising would produce pain.

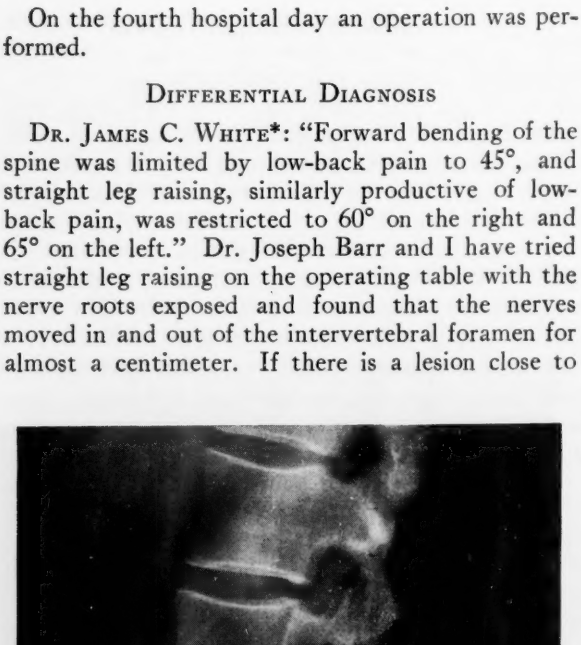

Figure 2. *Lateral View of the Lumbar Spine. Arrows indicate pressure erosion of the posterior aspect of the bodies of the second and third lumbar vertebras.*

"Pressure over the lumbar spine gave rise to pain in the buttocks." This also would indicate that the sacral roots were pressed on in some way.

"The right knee jerk was less active than the left, which was normally active. The ankle jerks were absent. The plantar reflexes were normal." Again, that would suggest a lesion of either the low lumbar or sacral nerves. I think most important for the knee jerk are the third and fourth lumbar roots, and for the ankle jerk, the first sacral. There was no suggestion of impairment of the corticospinal tract above.

If the urine was a catheterized specimen, one would think of cystitis as the cause of the frequency rather than a neurogenic disturbance.

Dr. Tracy B. Mallory: That urinalysis was done on admission. A catheterized specimen later showed 6 white cells per high-power field, an occasional red cell and a few bacteria.

Dr. White: Early pressure on the second, third and fourth sacral roots is likely to cause a little frequency and impairment of bladder function before the development of incontinence or inability to void.

May we see the x-ray films now?

Dr. Stanley M. Wyman: The films of the chest reveal no localized active disease. The spine shows very definite changes from the second to the fourth lumbar vertebra, characterized by thinning of the pedicles and widening of the interpedicular spaces. These changes are most marked at the third lumbar vertebra. They are well seen on the lateral views. There is quite an appreciable erosion defect on the posterior aspect of the third and to a lesser extent on the second lumbar vertebra.

Dr. White: It seems to me that we can say that the signs point clearly to an expanding mass within the spinal canal at the level of the cauda equina. There was just the one occasion when the hands felt slightly numb that makes one have some suspicion that this lesion involved anything higher than the cauda equina. However, I think that could have been on a functional basis. We have to concentrate on the lumbar vertebras and cauda equina and would expect probable damage to the sacral roots and to the second, third and fourth lumbar roots. That is perfectly possible with a lesion anywhere below the second lumbar vertebra.

To go over the various possibilities, likely and unlikely: the onset at the time of pelvic operation suggests the possibility of sepsis, perhaps an epidural abscess or osteomyelitis. There was no evidence of chronic osteomyelitis in the vertebras. An epidural abscess, as far as I know, never becomes chronic, although cases of long-standing pachymeningitis that might have begun in that way have been reported.

Spinal fluid could not be obtained on a lumbar puncture, which was done outside, so that we wonder if there was a large tumor that blocked the end of the needle when it was inserted through the dura and arachnoid. We do not know how many of these spaces had been tapped. At times a lumbar puncture — for example, between the fourth and the fifth lumbar vertebras — has been unsuccessful, but fluid has been obtained with only a slight rise in protein at the space above and fluid with a very high protein indicating obstruction from the space below, so that the lesion was at the fourth lumbar interspace. It was not really necessary to put this patient through a spinal puncture at the third lumbar or first sacral segment because the signs and the x-ray changes were so definite. It looks as though there was a particularly characteristic picture of tumor of the cauda equina of long duration.

*Chief of neurosurgery, Massachusetts General Hospital.

This nineteen-year history certainly ought to rule out any malignant lesion like carcinoma, sarcoma, melanoma or Hodgkin's disease. Chronic inflammation like tuberculous granuloma or pachymeningitis also would be rather unlikely. I have seen an echinococcus cyst that had been present for a long time in the subdural space, but there is nothing to indicate that here. From the x-ray films, if this were a briefer history I would think of neurofibroma or meningioma, although neurofibroma rarely extends over more than one vertebra. A meningioma could spread over a wider area, but the meningiomas that I have seen have been limited fairly well to a single vertebra. The most common tumor that involves a long extent of the cauda equina is an ependymal glioma, but it is not of such long duration.

We will have to think about rarer possibilities, and there are a number of these to consider. Elsberg et al.[1] and Turnbull,[2] in Vancouver, have reported epidural cysts, which may extend over an area this size, but they occur more often in adolescence. In Cloward's[3] cases of epidural cysts there was a forty-three-year-old man, but this is rather rare. There are usually some scoliosis or kyphosis and some postural mechanical changes in the spinal column with this lesion.

The congenital lesions can be of long standing. However, there is no mention about any overlying cutaneous dimple here. Furthermore, the patient had no spina bifida. Epidural lipomas and intradural lipomas too have been found in this area. Ehni and Pugh,[4] at the Mayo Clinic, reported a number of cases of such lipomas a few years ago. Dermoid cysts containing hair and epidermoid cysts containing cholesterol crystals can get mixed among the roots of the cauda equina and filum terminale, can extend up and down along the roots, and can produce long-standing symptoms of the type we see here. Boldrey[5] and List,[6] of Ann Arbor, have reported them. And teratoid tumors with all three germinal layers represented, I think, are not unusual in the spinal canal, but they usually have cutaneous outcroppings. I know that Scoville[7] described an intradural hemangioma, and Turner and Kernohan,[8] at the Mayo Clinic, have reported on some of these. They may extend over long areas in this region, but are pretty rare.

In summary, it seems to me that the duration of nineteen years rules out any malignant tumor and also an ependymal glioma. Ependymal glioma would be my first choice if the history were shorter. Angiomas are rare, and neurofibromas and meningiomas are not likely to extend over so many vertebras. Going out of the line of the commonest lesions, I believe, if one has to make a differential diagnosis of the histologic type of tumor, that an intradural epidermoid or dermoid cyst would be the best bet for a lesion involving three vertebras and existing for nineteen years.

Dr. H. Thomas Ballantine: We thought just as Dr. White did that this was undoubtedly a tumor of long standing involving the roots of the cauda equina primarily, with no pressure on the spinal cord itself, and I must confess that this is as far as we went. We did not attempt to elucidate the histology too much prior to surgery, although we believed that the history was confused, and it was by no means certain that the back pain and other numerous complaints over the period of nineteen years were entirely due to spinal-cord tumor.

A Physician: Was the cerebrospinal fluid from the cistern examined at all before operation?

Dr. Ballantine: No. Two well known neurosurgeons had made several attempts to obtain spinal fluid by the lumbar route. We did contemplate either a cisternal puncture or a high lumbar puncture, but as soon as we saw the x-ray films the diagnosis of tumor became obvious and we elected to operate.

Clinical Diagnosis

Tumor of cauda equina.

Dr. White's Diagnosis

Intradural cyst of cauda equina, ?epidermoid, ?dermoid.

Anatomical Diagnosis

Meningioma, region of cauda equina.

Pathological Discussion

Dr. Mallory: Dr. Ballantine, would you tell us what you found at operation?

Dr. Ballantine: A laminectomy was carried out from the first lumbar to the first sacral segment. The laminectomy was begun at the third lumbar segment, and the first thing that we saw was a very definitely eroded lamina. When the laminar plate, a very thin plate of bone, was lifted off, tumor presented out of its capsule and had actually eroded through the dura and come out into the spinal canal in the area. That was the reason for the thinning of the pedicle at the third lumbar vertebra. We then continued the laminectomy and found the entire cauda-equina region of the lumbar sac filled with this tumor. It was dark and well encapsulated, and we thought at the time that it was probably a meningioma. The nerve roots were pressed against the walls of the spinal canal, and the tumor occupied most of the center of the spinal canal. It was remarkable to us that the patient had any function at all in the nerve roots. The resection was begun, and the entire tumor removed in one piece except for the little excrescence that had penetrated the dura and had to be removed as a separate specimen.

Dr. White: What about a dural attachment?

Dr. Ballantine: We never found any obvious dural attachment. We believed that the area where the tumor had perforated the dura at the third lumbar vertebra might have been the original at-

tachment and we removed the dura in that particular spot.

The patient has been completely relieved of the back pain, but has some increased weakness of the right ankle.

DR. WHITE: Did Dr. Kubik substantiate that it was a meningioma?

DR. CHARLES S. KUBIK: Yes, that was right. I also thought before the operation that the early symptoms, which began so many years previously, might not have been due to the tumor and that the most likely diagnosis was ependymoma. As I recall it the patient began to have severe pain about four years before admission.

I have another lantern slide that we might show. This was an ependymoma removed from a patient who had had symptoms for nine years. The tumor completely filled the lumbosacral canal and extended into the lower part of the conus. These are probably tumors of the filum terminale, and although they are glial tumors many of them are encapsulated and can be successfully removed. This patient also had rather slight neurologic signs and had also been treated as a case of psychoneurosis up to about a month before she was admitted here.

DR. BALLANTINE: I wonder if we could have the exact dimensions of this tumor.

DR. MALLORY: It measured 9.8 by 3 by 2 cm.

DR. WHITE: Does Dr. Kubik recall any meningiomas that have extended over more than one vertebra?

DR. KUBIK: No; I do not recall any others.

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CASE 36402

PRESENTATION OF CASE

A seventy-year-old man was admitted to the hospital because of frequency and nocturia.

The patient had had nocturia and frequency for about twenty years, but in the month preceding entry these symptoms had increased in severity. In addition he had difficulty in starting the urinary stream. There was no history of hematuria. During the same period he had noticed increasing constipation, with considerable tenesmus, and had passed only small, somewhat loose, yellowish stools. He described the feeling that the stools were sticking in the rectum. There was no history of blood in the stools. He had occasional episodes of vomiting that he said followed a feeling of filling up although he denied nausea or anorexia. He had had minimal dyspnea, without chest pain or other cardiac symptoms. He had noted no weight loss.

On physical examination he appeared somewhat weak. Most of the teeth were missing and were not replaced by dentures. The lungs were clear to percussion and auscultation. The heart was enlarged to the left, with the apex in the anterior axillary line. The rate was irregular at 115 apparently with fibrillation. The abdomen was moderately tympanitic and slightly distended. Peristalsis was good. There was some tenderness over the left colon. No masses were palpated. The initial rectal examination showed a walnut-sized, stony-hard, nonmovable mass in the right posterior part of the prostate. On later examinations this was not so clearly defined, and it seemed to become much softer with repeated examinations. However, numerous prostatic calculi were readily identified by the examining finger, and the right seminal vesicle was described as enlarged.

The temperature was 99.6°F., the pulse 115, and the respirations 22. The blood pressure was 170 systolic, 90 diastolic.

Examination of the urine showed it to be cloudy, to have an acid reaction and a specific gravity of 1.028 and to give a ++ test for albumin and an olive-green reaction for sugar. No acetone or bile was present. The sediment contained 15 red cells, 20 white cells and 5 epithelial cells per high-power field, bacteria and mucin. Catheterization after complete voiding produced 40 cc. of urine. The white-cell count was 15,000, and the hemoglobin 14 gm. per 100 cc. The nonprotein nitrogen was 48 mg., the total protein 8.0 gm., and the alkaline phosphatase 2.4 units per 100 cc., and the carbon dioxide 31.9 milliequiv. and the chloride 91 milliequiv. per liter, and the prothrombin time 54 per cent of normal.

The distention of the abdomen decreased on the first hospital day, but on the following day the patient again became distended. Following an enema given in the evening in preparation for excretory urograms he became markedly distended, with bursts of high-pitched peristalsis and a feeling of fullness and nausea without pain. He began to vomit small amounts of gastric contents. The return from the enema was described as clear, and the amount returned complete. Plain films of the abdomen showed dilated loops of small bowel consistent with incomplete obstruction of the ileum. X-ray films of the chest were not remarkable, and a metastatic series showed no bone destruction. Calcification was noted in the prostate. A Harris tube was passed, and he was placed on continuous

suction and oral feeding was discontinued. The excretory urogram was canceled. On the following day he remained distended in spite of 600 cc. of gastric drainage. He began to have some cramping pains and to show some generalized abdominal tenderness. The blood pressure dropped to 135 systolic, 70 diastolic, and the heart rate jumped from 115 to 160 with a totally irregular rhythm. Peristalsis remained high pitched but did not impress the observers as obstructive in type. The temperature had remained normal. Catheterization yielded 300 cc. of residual urine and an indwelling catheter was left in place. Mottling of the skin that had not been present previously was noted. A cardiac consultant thought the heart was not enlarged. The sounds were of good quality, and there was a Grade II apical systolic murmur and a to-and-fro sound along the left sternal border at the third interspace that varied with respiration and seemed to be more characteristic of a friction rub than a murmur. The rhythm was totally irregular. Digitalization was carried out. The liver could not be felt because of the abdominal distention. The patient suddenly developed a temperature of 105°F. The abdomen was mottled and cyanotic, especially at the umbilicus, and the tympany and high-pitched peristalsis were still present. An abdominal tap yielded 5 cc. of frankly yellow pus. On smear this showed many neutrophils, some containing gram-positive cocci tending to form chains. At this time the nonprotein nitrogen was 54 mg. per 100 cc., and the carbon dioxide 32.3 milliequiv., the chloride 88 milliequiv. and the sodium 134 milliequiv. per liter, and the amylase 32 units per 100 cc. An electrocardiogram following partial digitalization disclosed a regular rhythm at a rate between 140 and 150. X-ray films of the abdomen again showed small-bowel distention with no essential change. The patient was given penicillin and streptomycin. The blood pressure fell to 80 systolic, 40 diastolic, and then to 60 systolic, 40 diastolic, although the pulse slowed and became more regular. The patient's condition continued to decline, and he became comatose and died early in the morning of the fifth hospital day.

Differential Diagnosis

Dr. Lorande M. Woodruff*: In review, this seventy-year-old patient came to the hospital with complaints of frequency, nocturia and some difficulty in starting the urinary stream; these symptoms are all consistent with a mild degree of low urinary-tract obstruction. The only other symptoms were related to the gastrointestinal system. He had vomiting occasionally following a feeling of filling up, some constipation and tenesmus, all perhaps pointing to an obstructive or irritative lesion in the lower rectal segment.

*Assistant in urology, Massachusetts General Hospital.

On physical examination he did not appear acutely ill, but was described as being weak. The heart was perhaps enlarged although I think it was normal on x-ray examination. The rate was rapid, and the heart was fibrillating. The lungs were clear. He evidently had no edema and was not in cardiac failure. In the abdomen there was a slight tenderness and moderate tympany. Peristalsis was good, and there were no masses. There was some tenderness over the left colon. There was nothing to give any clue that this patient was about to be so extremely ill that he would die within four days. On rectal examination a large mass was found in the posterior part of the prostate. Within the mass was a walnut-sized area that was nonmovable and stony hard. On repeated examinations this became much softer and much less clearly defined, and finally prostatic calculi were felt.

Examination of the urine showed evidence of concentration, and there were white cells, red cells and bacteria in the sediment, all of which are consistent with urinary infection. The albumin may have been due to the cells in the sediment. The olive-green sugar reaction on one determination is hard to evaluate, but since he had no acetone and was not in acidosis, he probably did not have diabetes. The white-cell count of 15,000 was further evidence of infection. The total protein was 8 gm., which makes one think that he had a certain degree of hemoconcentration, and as a result of that the nonprotein nitrogen of 49 mg. per 100 cc. was probably normal. The carbon dioxide and chloride point mainly to a slight degree of alkalosis.

For one day in the hospital the patient seemed to do well and the distention decreased, but on the next day he again became distended and that afternoon was given an enema. It was at about that time that the fireworks began. He became nauseated, vomited and had high-pitched peristaltic rushes, and became more distended. A Harris tube was passed, with little noticeable effect, and by the third day there was generalized abdominal tenderness, crampy pain and high-pitched peristalsis not obstructive in character. The blood pressure started to fall. On the following day the temperature rose to 105°F. He was still distended, and an abdominal tap showed 5 cc. of frankly yellow pus. The patient's condition continued to deteriorate, the blood pressure fell, and he died.

On the x-ray examination there were areas of calcification in the bladder or prostate. The patient was not cystoscoped. May we see the x-ray films now?

Dr. Stanley M. Wyman: As the record states, the chest was not remarkable. The heart is within normal limits for a person of this age. The aorta is somewhat tortuous. The first film of the abdomen shows a large quantity of gas, which appears to be almost entirely within loops of small bowel. The calcifications are well seen and are consistent with

prostatic stones. The films of the abdomen taken the next day show no essential change. There is very little gas in the ascending and the descending portions of the colon. On the following day there seems to be some fluid between loops of small bowel suggesting free peritoneal fluid. On the same day a film taken in the upright position shows pronounced fluid levels in the small bowel.

DR. WOODRUFF: Thank you.

I think the patient died with a generalized peritonitis. The evidence for this is the marked distention and generalized abdominal tenderness, high-pitched peristalsis, not obstructive in type and, I suppose, greatly diminished, and finally the abdominal tap that yielded 5 cc. of pus. To obtain 5 cc. of pus, a localized abscess must be tapped, or a considerable amount of pus must be present. With an infection that was so sudden and so overwhelming, one immediately thinks of a rupture of some hollow viscus, such as a perforation of a gastric or duodenal ulcer, of the gall bladder, of the appendix or of a carcinoma of the cecum, all of which could give rise to a prompt, rapidly spreading peritonitis. There was no history, however, of any one of these conditions. At the time of admission, there were no symptoms that would lead one to make a diagnosis of any of these conditions, and finally there were no physical findings. At no point was there any abdominal mass. There was some localized tenderness in the left colon on admission, but that is not mentioned again and seems quite indefinite. Also, this infection, from a smear of the pus, was said to be of a coccal type. That is against its arising from a rupture of some intestinal organ. From the history it appears that soon after or during the enema the patient became much worse. The distention, however, had been present all that day. Although it is possible that the enema caused some perforation in the bowel, there is not much evidence to bear it out. I believe the distention that had been going on all day was merely accentuated at the time of the enema.

A ruptured urinary bladder could cause a spreading peritonitis, but there was no history of trauma. Although an instrument was passed, it was presumably a soft catheter, which, unless the wall had been greatly weakened by carcinoma, would not rupture the bladder. When the bladder ruptures, the passage of acid urine onto the peritoneal surface usually gives rise to sudden acute low abdominal pain, increasing in severity together with abdominal rigidity. This is quite unlike what this patient had. Later, he was again catheterized, and 300 cc. of urine was obtained from the bladder so that the bladder must have remained fairly intact.

The mass in the prostate was unusual to say the least. I am interested to see how much calcification there is in the x-ray films. The calcifications are spread over a very large area, are irregular in size and shape and are consistent with calculi in the prostate. Some of them could be in the bladder. The description of a stony-hard mass in the prostate brings to mind immediately a carcinoma of the prostate, but that never softens under pressure so I can exclude that.

An area of inflammation could be stony hard, but that again would not be expected to soften. I interpret this softening to mean that there was quite a change, and I wonder if this patient did not have an abscess that was tense at the time it was first examined and that later ruptured and became softer and less clearly defined. I am surprised that an abscess should not be tender. Abscess of the prostate usually ruptures into the urethra, with discharge of the pus into the urine and relief of symptoms. Frequently an abscess of the prostate is moderately silent for long periods, and it is only after extension of infection into the urinary tract, with cystitis and pyelonephritis, that symptoms arise. Although these abscesses usually rupture into the urethra, I see no reason why an abscess near the posterior portion of the gland, particularly if blocked from the urethra by a large amount of hyperplasia, could not rupture posteriorly. If it did, it would be in immediate relation with the peritoneum. The anterior and posterior leaves of the peritoneum fuse at the upper border of the prostate to form the pouch of Douglas, so that the seminal vesicles and the prostate are in immediate relation with this pouch.

This patient had a long-standing chronic infection, as shown by the presence of all these stones. I am inclined to say that there was either a cyst or an abscess of the prostate or the seminal vesicles. I believe that cyst or abscess of the seminal vesicles is very uncommon, and there is really nothing pointing to it. There was, however, evidence of a large amount of calcification in the prostate. I would expect a cyst to be fluctuant, and there was no evidence of that.

My diagnosis is prostatic abscess, with rupture and generalized peritonitis.

Dr. John T. Quinby: Would you think that this man could have had an infectious process in the bowel, such as diverticulitis, with rupture or an appendiceal abscess, possibly with pylephlebitis?

Dr. Woodruff: Yes; I would, but I would say that with diverticulitis there should be a pelvic mass that could be felt. This mass is described as in the prostate.

Dr. Quinby: There was something that might have been in the pouch of Douglas that disappeared after the first rectal examination.

Dr. Woodruff: This description does not fit an inflammatory mass high in the pelvis but does fit one high in the prostate. The x-ray film shows a very large prostate filled with stones and infection. There was no history of diverticulitis.

Dr. Benson B. Roe: After the onset of the downhill course, I was asked to see the patient in consultation. At that time the clinical picture — the fibrillation, the somewhat insidious onset of symptoms and the not very dramatic abdominal tenderness — was consistent with a mesenteric thrombosis. The differential diagnosis between mesenteric thrombosis and peritonitis was settled by the abdominal tap. The pus, of course, established peritonitis as the disease. Because of the severe debilitation of the patient at that time we thought we should not explore, particularly without a very good idea of the probable source. Had he been in better shape, an exploration might have been warranted.

Dr. Ernest Craige: I was asked to see this patient because of the rapid fibrillation. He had no past history of heart disease, and there were no signs of cardiac impairment or murmur. He was given digitalis, and the rate seemed regular. It seemed to me that the cardiac condition was not of any great importance.

Dr. Wyman: I wonder if in addition to Dr. Quinby's suggestion of diverticulitis, which I rather favor, one might think of a silent carcinoma of the left colon that had perforated following the enema. I would prefer diverticulitis or perforating carcinoma to disease of the prostate.

Clinical Diagnoses

Abscess of prostate.
Generalized peritonitis.

Dr. Woodruff's Diagnosis

Abscess of prostate, with rupture and generalized peritonitis.

Anatomical Diagnoses

Diverticulitis of rectosigmoid, with abscess formation.
Generalized peritonitis.

Pathological Discussion

Dr. Tracy B. Mallory: The patient was discharged to the Pathology Department with the same diagnosis as Dr. Woodruff has made, prostatic abscess and generalized peritonitis. At autopsy, however, we found the alternative. He did have multiple diverticula of the large bowel and an abscess in immediate apposition with the prostate that evidently surrounded a perforated diverticulum. This had a thick, fibrous wall and had certainly been present for a considerable time. There was evidence of fresh dissection of the abscess upward and rupture into the peritoneum in the pouch of Douglas. The other findings at autopsy were insignificant. The heart was very slightly enlarged. For a man of seventy years he had extraordinarily little sclerosis, and the coronary arteries and myocardium were in almost perfect condition.

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MANKIND'S CONCERN

The new, stream-lined United Community Services organization of Metropolitan Boston will face its critical test this month.

Replacing the older Greater Boston Community Fund and Greater Boston Community Council, the present organization is the result of an exhaustive study, conducted from 1947 to 1949, of the unique conditions that have existed in and about charitable-minded Boston for decades. The outcome of the survey was the elimination from the major money-raising campaign of many appeals for funds where functions were duplicated and purposes overlapped.

Even now, composing this major representative of the 1250 Red Feather organizations of the country, are over 300 agencies devoted to the steady day-in and day-out health and social needs of forty-eight of the communities that make up Greater Boston.

The United Community Services campaign that is at this time being put on foot *must* succeed; the needs of the communities *must* be met; the thousands of workers who are striving in the interests of humanity *must not* be discredited. Competitive appeals constitute one of the great hazards to the success of the campaign, but its greatest is the indifference of the large, solvent majority of the public to the needs of its less fortunate fellows. Man's inhumanity to man makes countless thousands mourn indeed.

And where, in this major humanitarian effort, stands that select body of public-spirited and civic-minded citizens, the physicians? Figures relative to them are available for the fund-raising campaign of 1948, when, of the physicians in the area, 1127 made some sort of contribution and 651, or 36.7 per cent, made none.

Of the contributors, 623, or 55.2 per cent, gave $25 or more; 371, or 33.0 per cent, gave $50 and over, and 212, or 18.8 per cent, gave $100 or more.

The majority of physicians, as they truly state and as is generously recognized, give more or less largely of their time and skill to charity, and for this they should be commended in due measure. In this commendation, however, one must not forget the business men and women and the members of other professional and domestic groups, who, mindful of their obligations to society, give also of themselves as well as of their money in countless enterprises devoted to service.

Too many persons are oblivious of their neighbors, and others will go with them only the first mile. The second is traveled by all who are fully conscious of their place in a world that can be improved only by united effort. In this chosen group every physician should be found.

SENDING IN THE SUBSTITUTES

On August 23, as previously reported in the *Journal*, a telegram from medical schools and hospitals in Massachusetts was dispatched to the Secretary of Defense and the chairmen of the National Security Resources Board and Senate Armed

Services Committee urging immediate passage of the draft law. Early in September the measure was passed by Congress and signed by the President. As pointed out in the telegram, the new legislation avoids the necessity of coercing young men into military service before the responsibility for a clear-cut manpower policy is accepted by the nation's leaders. The new law appears to be both a fair and a practicable way of calling doctors to military service. Furthermore, should total war suddenly erupt from the blaze in Korea, it also paves the way for increasing the supply at a greatly increased tempo. The practical challenge now is to see that the law is speedily implemented by civilian and military authorities.

Before passage, and after the bonus bribe had failed to fill military quotas, the papers were fond of using the term "prodding" the doctors into the service, and much was written about the particular necessity of prodding those "trained at Government expense but who had no previous active duty." Actually, the handling of these young men never offered any problem. Theirs was, and is, the clearly manifest duty to furnish the great majority of company-grade officers for field and hospital dispensaries and services, and without bonuses. If the young doctor has hung back from volunteering, it was because, like most other doctors in the country, he was, in his own opinion at least, engaged in an indispensable part of his training or indispensable to some group or project as regards medical services and waiting one more day, one more week, one more month to learn what the over-all plans were — the administration plan, the armed forces plan and the doctors' plan. He is the first to admit that, when the big draft is on, his middle name is "Available."

But the A.S.T.P. and V-12 groups cannot furnish leadership, which must come from those mostly between thirty-five and fifty-five years of age, many of whom have seen prolonged military service at one time or another — and many of whom have not. The easy and quick way and perhaps for a few weeks the only way to get the requisite number of doctors into service will be to "call up the reserves." There are many who saw two, three or four years' service in World War II who would step forward voluntarily and without bonuses the instant Russia moved in strength, but at this stage of subtotal warfare are thinking that if it is a question of drafting doctors during these years of siege, those who served in the last war should not be discriminated against.

Able-bodied physicians who saw no service can be called upon to assume their share of the medical contribution nearly as quickly as those whose names were on the files from 1941 to 1945. The latter physicians, whose patriotism is a matter of record, resent receiving orders and being almost literally "prodded" to active duty in quite a different order of priority from that stated in the law — a law that is considered on all sides to be fair in principle. Its speedy implementation is as much to be desired now as fair and effective enforcement; now is the time for the defensive team to get into the game. That's modern football — and war.

BRUCELLOSIS

THAT brucellosis is a problem in New England is shown by the fact that, for the seven-year period 1940 through 1946, Vermont had the highest average annual rate in the United States (18.5 per 100,000) and Connecticut (5.4 per 100,000) was eighth on the list of states. Yet brucellosis is a preventable disease provided that the spread of organisms from animal to man can be prevented. Infected animals, not sick people, are the reservoirs of infection.

The only contact of most people in the United States with farm animals is through the consumption of dairy products, and the only vehicle seriously implicated in the spread of brucellosis is milk. Since milk is usually pasteurized, the part of the population exposed to infection is readily limited to rural consumers of raw milk and certain occupational groups such as veterinarians, packing-house employees and farm workers.

The control of animal brucellosis has been entrusted, by law, to the Department of Agriculture, which developed an extensive test-and-slaughter program during the early thirties. This had the dual objective of cutting down surplus numbers and at the same time getting rid of diseased animals. Economic conditions of those times made the farmers amenable to this approach, and from

1934 to 1940 bovine brucellosis was cut in half, or from 10 per cent to 5 per cent of the cattle. With hostilities in Europe and the rise in prices for livestock and fodder, farmers were not so quick to subscribe to a program that might decimate their herds. This attitude neglects consideration of economic losses from the disease (estimated at $100,000,000 annually), although it has a certain rough-and-ready justification in times of full production. Long-term policy may be modified from time to time by such temporary considerations, but should not be determined by them.

All during World War II, and since then, agriculture has vacillated between two methods of brucellosis control: slaughter of the diseased animals, as practiced against contagious pleuropneumonia, foot-and-mouth disease and bovine tuberculosis; and compromise measures such as immunization and isolation applied to the control of hog cholera and bovine mastitis. Veterinarians are about equally divided in their opinions about the relative merits of these two systems, each of which has its place in animal husbandry.

A further advance in knowledge is needed to settle the controversy and the publication* by the American Association for the Advancement of Science of the papers presented at a symposium on brucellosis, sponsored jointly by the National Institutes of Health of the United States Public Health Service, the United States Department of Agriculture and the National Research Council, is evidence of the great amount of work being done on all phases of the subject.

The United States Livestock Sanitary Association has promulgated four plans of control: test and slaughter of reactors with or without vaccination of calves; test and retention of adult reactors with vaccination of calves; vaccination of calves without any testing program; and vaccination of adult animals. Of these, the last three are visualized as temporary expedients to tide an individual farmer over a period when the incidence of the disease is high among his animals. It is apparent that the only plan consistent with the theoretical objective of eradication is a sustained application of a test-and-slaughter program. That this approach is feasible is indicated by the fact that North Carolina and New Hampshire are certified as modified accredited areas with less than 1 per cent brucellosis in cattle and that Maine is well on its way to becoming the third accredited state.

The problem of brucellosis not only is a matter of dealing with the 5 per cent of infected cattle but also involves the protection of the 95 per cent of negative reactors distributed among 80 per cent of the herds now free of disease. A test-and-slaughter program, though a costly measure, may yet prove most economical from a long-term point of view. It is the method that gives promise of effecting the eradication of brucellosis from herds on a regional or national scale.

**Brucellosis, a Symposium.* 271 pp. Washington, D. C.: American Association for the Advancement of Science, 1950.

RODENT ULCER

WISCONSIN is a state that has long been noted for its dairying industry and in particular for its fine cheeses; this fact may in part account for the interest that has been taken over a long period of time by the University of Wisconsin in rodents — their natural history, their eating habits, their social life and their extermination.

As long ago as 1948, in the first half of the present century, a news release from the University of Wisconsin revealed the results up to that time of this long-term study. The habits of rats and mice were then given publicity and various methods of annihilating them were discussed. Although, in this report, the electric eye and the ingenious devices that depended on it were featured heavily for mass extermination, the house cat (*Felis libyca domestica*) and the snap trap seemed still to be the steady, all-season, reliable eliminators.

Somewhat as a side issue but seemingly necessary in order to make the investigation scientifically complete, the Wisconsin rodentologists later made available the results of a fascinating excursion into the club life of the bat. These placental mammals, however, are not of the order of rodents at all, belonging rather to that of *Chiroptera*, with forelimbs modified to form wings. The common designation of these furry fliers as flittermice led naturally to the error. The great mystery of bat life is the

propensity of the males to hibernate in otherwise abandoned belfries while the females are elsewhere.

The latest release from Madison announces the results of field tests with Warfarin (formerly known as W.A.R.F.-42 or Compound 42). This chemical, with a high safety factor for human beings and domestic animals, is considered to be one of the most effective means of rodent control yet discovered, killing its victims by producing hemorrhage. Tasteless and odorless to rodents, it is a slowly acting poison that must be consumed over a period of several days to cause death. Its nontoxicity in single doses is responsible for the high margin of safety, as the danger of a child, pet or domestic animal consuming the bait over a number of days is relatively small.

The field trials with Warfarin have been successfully conducted in practically every state in the Union, as well as in Canada, Hawaii and elsewhere overseas, so its value is not limited to the indigenous vermin of Wisconsin.

The annual expenditure in England for spirits, beer, tobacco and snuff, amounts to upwards of fifty-seven millions sterling.

Boston M. & S. J., *October 2, 1850*

BOSTON MEDICAL LIBRARY

NOTES

Dr. Henry R. Viets, librarian, is an associate editor for the United States of the new international periodical, *Centaurus*, devoted to the history of medicine and science. It is published in Copenhagen, Denmark, by Ejnar Munksgaard, and is under the editorship of Jean Acker. The first number was issued in August, 1950.

James F. Ballard, director of the Library, is an associate editor for the United States of the new periodical, *Libri, International Library Review*, devoted to bibliography and librarianship. It is also published in Copenhagen, by Munksgaard, under the editorship of Jean Acker, director of the medical and scientific department of the university at Copenhagen, and Svend Dahl, director of the Royal Library, Copenhagen. The first number was published in August, 1950, and contains original articles on bibliophiles in ancient Rome, notes on the Farmington plan by Keyes D. Metcalf and Edwin E. Williams, director and staff member, respectively, of the Harvard University library, the German bibliographic situation of the present time, the dawn of library consciousness, by S. R. Ranganathan, president of the Indian Library Association and a recent visitor to Boston, and a short article on a manuscript of Jean Grolier in the Austrian national library. Mr. Ballard will be pleased to receive and consider manuscripts on bibliography and bibliographies, and on the various aspects of librarianship, either general or special.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR AUGUST, 1950

RÉSUMÉ

DISEASE	AUGUST 1950	AUGUST 1949	SEVEN-YEAR MEDIAN
Chancroid	0	1	1*
Chicken pox	190	221	163
Diphtheria	6	25	17
Dog bite	1324	1238	1025
Dysentery, bacillary	7	2	12
German measles	63	117	47
Gonorrhea	260	258	365
Granuloma inguinale	0	0	0*
Lymphogranuloma venereum	0	1	1*
Malaria	0	1	13
Measles	317	151	274
Meningitis, meningococcal	3	5	5
Meningitis, Pfeiffer bacillus	4	0	1
Meningitis, pneumococcal	0	1	1
Meningitis, staphylococcal	0	0	0
Meningitis, streptococcal	0	0	0
Meningitis, undetermined	7	5	4
Mumps	268	275	273
Poliomyelitis	99	719	80
Salmonellosis	12	73	24
Scarlet fever	53	66	110
Syphilis	87	153	293
Tuberculosis, pulmonary	181	223	233
Tuberculosis, other forms	13	7	13
Typhoid fever	5	3	4
Undulant fever	3	2	5
Whooping cough	379	479	475

*Six-year median.

COMMENT

The only disease notably above the seven-year median was measles. Below the seven-year median were diphtheria, gonorrhea, salmonellosis, scarlet fever, syphilis and whooping cough.

The ninety-nine cases of poliomyelitis represented a prevalence above the seven-year median, but far below the number of cases reported in August, 1949.

Diphtheria had the lowest reported incidence for the month of August in six years.

Although August is the low month in the seasonal incidence of scarlet fever, 53 cases is the lowest monthly report in records of the past forty-five years.

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Diphtheria was reported from: Arlington, 1; Boston, 1; Chelsea, 1; Lowell, 2; Somerville, 1; total, 6.

Dysentery, amebic, was reported from Springfield, 1; total, 1.

Dysentery, bacillary, was reported from Belchertown, 2; Boston, 1; Danvers, 1; Lynn, 1; Worcester, 2; total, 7.

Encephalitis, infectious, was reported from Cambridge, 1; Shrewsbury, 1; Waltham, 1; total, 3.

Hepatitis, infectious, was reported from Amesbury, 2; Cambridge, 1; Maynard, 1; Wrentham, 2; total, 6.

Lymphocytic choriomeningitis was reported from Cambridge, 1; total, 1.

Meningitis, meningococcal, was reported from Cambridge, 1; Mansfield, 1; Springfield, 1; total, 3.

Meningitis, Pfeiffer bacillus, was reported from Boston, 1; Fitchburg, 1; Northampton, 1; Quincy, 1; total, 4.

Meningitis, mumps, was reported from Medford, 1; Newton, 1; Waltham, 1; total, 3.

Meningitis, salmonella, was reported from Boston, 1; Wareham, 1; total, 2.

Meningitis, undetermined, was reported from Barnstable, 1; Fall River, 1; Foxboro, 1; Lynn, 1; Medford, 1; Northampton, 1; Quincy, 1; total, 7.

Poliomyelitis was reported from: Amesbury, 1; Amherst, 1; Arlington, 1; Attleboro, 2; Belmont, 1; Boston, 6; Bourne, 3; Braintree, 3; Brockton, 1; Brookline, 1; Chicopee, 1; Easton, 1; Everett, 1; Fall River, 2; Falmouth, 1; Fitchburg, 2; Framingham, 1; Franklin, 1; Groton, 1; Haverhill, 1; Hingham, 2; Hinsdale, 1; Leominster, 1; Lynn, 6; Malden, 4; Manchester, 1; Marblehead, 3; Mattapoisett, 1; Melrose, 1; Milton, 3; Needham, 1; Newton, 5; North Andover, 1; Northampton, 1; Norwell, 1; Norwood, 1; Palmer, 1; Pittsfield, 8; Quincy, 6; Randolph, 1; Salem, 2; Southwick, 1; Springfield, 3; Stoneham, 1; Sturbridge, 1; Tisbury, 1; Wakefield, 1; Waltham, 1; Wareham, 1; West Springfield, 2; Weston, 1, Weymouth, 2; Williamstown, 1; total, 99.

Salmonellosis was reported from Arlington, 1; Boston, 4; Brookline, 2; Holyoke, 3; Lowell, 1; Newton, 1; total, 12.

Septic sore throat was reported from Boston, 3; Fall River, 1; total, 4.

Tetanus was reported from Billerica, 1; total, 1.

Trichinosis was reported from Boston, 2; Weston, 3; total, 5.

Tularemia was reported from Gay Head, 1; total, 1.

Typhoid fever was reported from Billerica, 1; Boston, 3; New Bedford, 1; total, 5.

Undulant fever was reported from Gloucester, 1; North Andover, 1; Wrentham, 1; total, 3.

CORRESPONDENCE

OFFICERS OF BOARD OF REGISTRATION IN MEDICINE

At the annual meeting of the Board of Registration in Medicine held on Thursday, July 20, 1950, the following officers were elected: Dr. Anthony O. Cardullo, chairman; Dr. George L. Schadt, secretary.

GEORGE L. SCHADT, M.D.
Secretary

State House
Boston

NOTICES

ANNOUNCEMENTS

Dr. J. Roswell Gallagher announces the removal of his office to Davison House, Wesleyan University, Middletown, Connecticut, where he is now college physician.

Dr. Robert Shapiro announces the opening of his office for the practice of orthopedic and traumatic surgery at 314 Commonwealth Avenue, Boston.

INTERNATIONAL MEDICAL ASSEMBLY

The thirty-fifth International Medical Assembly, a postgraduate school of the Interstate Postgraduate Medical Association of North America, will be held on November 6, 7, 8 and 9 at the Hotel Stevens, Chicago. The general chairman is Dr. Warren H. Cole, President of the Chicago Medical Society.

MEDICAL INTERNSHIPS IN PUBLIC HEALTH SERVICE

The Public Health Service is offering 122 approved one-year rotating internships in eleven of its United States Marine Hospitals, to begin on July 1, 1951.

These internships are open to graduates of approved medical schools. Appointments are made on a competitive basis according to the Uniform Intern Placement Plan. Successful applicants must qualify for a commission as assistant surgeon in the Reserve Corps of the Public Health Service and express an intent to serve an additional year with the Public Health Service after completion of internship. After internship there are many and various opportunities in the Public Health Service in practically all fields of medicine, including clinical care of patients, research, preventive medicine and public health. In addition, the Public Health Service is the medical corps for the United States Coast Guard and supplies officers to the Point IV Program.

Applications and further information may be obtained from the Public Health Service, Federal Security Agency, Washington 25, D. C. (Attention: Chairman, Committee on Residencies and Internships).

COURSE IN TREATMENT OF PARAPLEGIA

A course in the treatment of paraplegia will be given at Cushing Veterans Administration Hospital, Framingham, Massachusetts, on alternate Wednesday evenings, beginning on November 29. There will be twelve sessions in all, each beginning at 7:30 o'clock and lasting for two hours and a quarter.

The course will be given by the staff of the Paraplegia Service, with the assistance of other members of the hospital's full-time and consulting staffs. It will be open to all physicians without cost. Those interested should communicate, before November 1, with Dr. H. S. Talbot, chief, Paraplegia Service, Cushing Veterans Administration Hospital, Framingham, Massachusetts.

SOCIETY MEETINGS AND CONFERENCES

OCTOBER 9–11. National Gastroenterological Association. Page 470, issue of September 21.

OCTOBER 9–20. New York Academy of Medicine. Page 430, issue of September 14.

OCTOBER 10. Massachusetts Society of Anesthesiologists. Page 430, issue of September 14.

OCTOBER 10. Springfield Academy of Medicine. Page 512, issue of September 28.

OCTOBER 12–14. American Association of Blood Banks. Page 428, issue of March 16.

OCTOBER 13. Chemotherapy — New Preparations, Their Efficacy and Effects. Dr. Chester S. Keefer. Pentucket Association of Physicians. 8:30 p.m. Haverhill.

OCTOBER 14–19. American Academy of Pediatrics. Page 962, issue of June 15.

OCTOBER 17. South End Medical Club. Page 512, issue of September 28.

OCTOBER 23–27. American College of Surgeons. Page xi, issue of June 29.

OCTOBER 23–28. Medicomilitary Symposium for Officers of Fourth Naval District. Page 34, issue of July 6.

OCTOBER 28. Massachusetts Association of Medical Technologists. Page 324, issue of August 24.

OCTOBER 30–NOVEMBER 3. American Public Health Association. Page 240, issue of August 10.

OCTOBER 31–NOVEMBER 3. International College of Surgeons. Page 170, issue of July 27.

NOVEMBER 1. New England Obstetrical and Gynecological Society. Hotel Somerset, Boston.

NOVEMBER 1. Hampshire District Medical Society. Page 170, issue of July 27.

NOVEMBER 5 AND 6. American Society for the Study of Arteriosclerosis. Page 170, issue of July 27.

NOVEMBER 6–8. New England Postgraduate Assembly. Hotel Statler, Boston.

NOVEMBER 6–9. International Medical Assembly. Notice above.

NOVEMBER 10. American Trudeau Society. Page 280, issue of August 17.

NOVEMBER 14. New England Society of Anesthesiologists. Page 512, issue of September 28.

JANUARY 31. American Academy of Orthopaedic Surgery (see Kappa Delta Award for Research in Orthopedic Surgery). Page 736, issue of May 4.

FEBRUARY 13. New England Society of Anesthesiologists. Page 512, issue of September 28.

(Notices concluded on page xv)

NOTICES (*Concluded from page 548*)

April 9–13. American College of Physicians. Page 962, issue of June 15.

April 10. New England Society of Anesthesiologists. Page 512, issue of September 28.

May 8. New England Society of Anesthesiologisst. Page 512, issue of September 28.

May 24–26. American Goiter Association. Columbus, Ohio.

District Medical Society

HAMPSHIRE

November 1. 4:30 p.m. Northampton State Hospital.
January 3. 4:30 p.m. Veterans Administration Hospital, Northampton.
March 7. 4:30 p.m. Cooley-Dickinson Hospital, Northampton.
May 2. 4:30 p.m. Annual Meeting. Jones Library, Amherst.

Calendar of Boston District for the Week Beginning Thursday, October 12

Friday, October 13

*9:00 a.m.–12:00 m. Combined Medical and Surgical Staff Rounds. Peter Bent Brigham Hospital.

*10:00 a.m. Surgical Clinic. South End Health Unit, 57 East Concord Street, Boston.

12:00 m.–1:00 p.m. Clinicopathological Conference (Boston Floating Hospital). Joseph H. Pratt Diagnostic Hospital.

*1:30 p.m. Tumor Clinic. Out-Patient Department, Mount Auburn Hospital, Cambridge.

Monday, October 16

*11:30 a.m.–12:15 p.m. Clinical Conference. South End Health Unit, 57 East Concord Street, Boston. Dr. Cleaveland Floyd in charge.

*12:15–1:15 p.m. Clinicopathological Conference. Main Amphitheater, Peter Bent Brigham Hospital.

Tuesday, October 17

*12:15–1:15 p.m. Clinicoroentgenological Conference. Peter Bent Brigham Hospital.

*1:30–2:30 p.m. Pediatric Rounds. Burnham Memorial Hospital for Children, Massachusetts General Hospital.

Wednesday, October 18

*12:00 m. X-Ray Conference. Margaret Jewett Hall, Mount Auburn Hospital, Cambridge.

*12:00 m.–1:00 p.m. Clinicopathological Conference. (Children's Medical Center.) Amphitheater, Peter Bent Brigham Hospital.

*Open to the medical profession.

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AT THE

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For further information apply to the Dean, Boston University School of Medicine, 80 East Concord Street, Boston, Massachusetts.

*There will be no exercise on November 8 because of the New England Postgraduate Assembly.

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